Dental Infections Oral and Systemic

(Volume I)
(Part II)

BEING A CONTRIBUTION TO THE PATHOLOGY OF DENTAL INFECTIONS FOCAL INFECTIONS, AND THE DEGENERATIVE DISEASES

BY

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THIS IS THE EXPERIMENTAL BASIS FOR VOLUME II

"DENTAL INFECTIONS AND THE DEGENERATIVE DISEASES"

VOLUME I
PARTS 1 AND II
PRESENTS

RESEARCHES ON FUNDAMENTALS OF ORAL AND SYSTEMIC EXPRESSIONS OF DENTAL INFECTIONS

VOLUME II
PARTS I AND II
PRESENTS
RESEARCHES ON CLINICAL EXPRESSIONS OF DENTAL INFECTIONS

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CHAPTER XXV.

THE RELATION OF THE TYPE OF REACTION TO THE NATURE OF THE IRRITANT, BACTERIAL OR TOXIC.

PROBLEM: Have we different products from dental infection?

EXPERIMENTAL AND DISCUSSION.

In Chapter 17, we have discussed the presence of non-bacterial poisons of dental origin; and in Chapter 24, we have discussed the quality of bacterial invasion and its elective localization. This research was undertaken to determine what, if any, relationship there is between the type of systemic disturbance and the nature of the irritant. One method of procedure has been to take from the teeth of patients suffering definite and acute systemic involvements, both the organisms growing therein, and the soluble poisons present in those teeth, and injecting these into experimental animals. In Chapter 18 under the discussion of "Studies of Pulpless Teeth," I presented a chart showing the effects on animals of injections with the washings from crushed infected teeth, both with and without filtering, and have compared these with the effects on animals of cultures grown from teeth (Figure 24, Chapter 2), either the same or similar ones, both when in media in which they were grown, and when removed from media and washed with several changes of normal salt solution and then inoculated in a normal salt solution suspension. By referring to those charts, it will be seen that the average length of life of animals injected with the washings of the teeth, was less in this group than in the groups inoculated with the washings plus the organisms, and also less than when injected with the culture of the organisms without the toxic substance from the tooth, whether the organisms were washed or injected in the medium in which they have grown. These figures were as follows:

The average length of life of 13 animals inoculated with filtered washings from teeth, was 5 days; as compared with the group with unfiltered washings in which 8 animals died with an average life of 12 days. In the third group of 8 animals, inoculated with the organisms washed and suspended in sodium chloride, the average

length of life was 7 days; and in fourth group of 71 animals, in two series, 16 in the first and 55 in the second, receiving whole culture, (these organisms in the medium in which they grew, approximately 1 cc. doses), in the first series of 16, the average length of life was 6 days, and in the second group of 55 was 7 days. In another chapter I have suggested an explanation for the phenomenon of the toxic substance killing in less time than the toxic substance plus the organisms producing it.

In our various efforts to study in a comparative way the injurious effects of toxins and bacterial invasions, the comparisons have been more largely between miscellaneously selected toxins and miscellaneously selected dental cultures. I have, accordingly, undertaken to check this more closely by extracting the toxin from given teeth for inoculation as washings from the tooth in one group of animals, in some cases filtered, others not filtered, and comparing these effects with homologous cultures by growing the organisms from the particular tooth from which the toxic substance had been washed. A group of these is shown in Figure 157. In the group showing changes in weight of rabbits inoculated with tooth washings, seven—namely, the sixth, seventh, eighth, tenth, eleventh, twelvth, and thirteenth,—were filtered washings, and the others of that group—namely, the first, second, third, fourth, fifth, and ninth, — from unfiltered. In this group the average loss in weight per rabbit was 131 grams and the average percentage loss 11½. In the group inoculated with the culture from these same teeth, the average loss of weight per rabbit was 180 grams and the average percentage loss 17. It will be noted that in this series the loss in weight was more rapid where they received the whole culture, that is 1 cc. of organisms and culture medium from a twenty-four hour growth, than where they received washings from the single tooth only. The difference, however, was one of degree, for the effects were very serious with both. This suggests that when a patient is receiving the toxic material into the system in addition to the bacterial invasion, the injury would be distinctly worse than to receive either one alone. It is of interest to note that in this group of nine rabbits inoculated with washings, the rabbit that lost the greatest amount, both in total grams and in percentage—namely, number eight—received a filtered washing. This corresponds with some of the data shown in other studies which demonstrates that the toxic material in some teeth is extremely injurious, for the length of time required

COMPARISON OF TOOTH TOXIN AND TOOTH CULTURE

A. Tooth Washings

Case No.	Rabbit No.	Tooth Washing Unheated		No. of Days Lived	Weight Changes					
					Gain		Loss		% Gain per day	% Loss per day
		Filtered	Unfiltered		Actual	%	Actual	%		
433	145		"	11			44	3.9		0.4
891	274		"	10			194	18.0		1.8
1014	285		"	6			170	19.4		3.2
1014	294		"	9			0	0.0		0.0
1081	288		"	11			90	9.4		0.9
1149	592	"		1			15	1.3		1.3
1149	593	"		14*			14	1.0		0.1
1157	542	"		4			278	24.0		6.0
1153	545		"	34*	124	10.4			0.3	
1171	607	"		11			510	34.5		3.1
1123	621	"		6			191	25.0		4.2
1177	640	"		7			263	21.0		3.0
1412	753	"		49*			59	4.9		0.1

B. Tooth Cultures

Case No.	Rabbit No.	Culture		No. of Days Lived	Weight Changes					
					Gain		Loss		% Gain per day	% Loss per day
		Whole	NaCl Suspension		Actual	%	Actual	%		
433	146	"		10			309	27.1		2.7
891	275	"		32*			334	25.9		0.8
1014	289	"		5			166	18.6		3.7
1014	293		"	22			227	30.6		1.4
1014	294		"	9			163	20.5		2.3
1081	291		"	43	10	1.3			0.1	
1149	594		"	11*			148	13.6		1.2
1149	595		"	13*			13	1.0		0.1
1149	596		"	10			535	39.6		3.9
1149	597		"	11*			105	11.1		1.0
1157	544		"	12			144	16.5		1.4
1153	549		"	9			230	24.5		2.7
1153	550		"	7			318	27.5		3.9
1171	606		"	14			174	18.5		1.3
1123	613		"	21*			73	6.0		0.3
1177	643		"	17*	154	14.5			0.9	
1412	755		"	9			329	31.0		3.4
	756		"	3			137	13.5		4.5

* Chloroformed

FIGURE 157.

for this rabbit to lose 24 per cent in weight was only four days. The average percentage loss per rabbit per day for the group receiving the washings was 1.8 and for the group receiving the inoculations of the cultures of the same teeth was 1.9 Another rabbit of this series, No. 592, receiving the filtered washings of a tooth, died in one day. On this account, it will be seen it is not sufficient to judge total loss, since a rabbit may be killed so quickly by the toxic substance of a filtered washing that it does not have time to lose in weight.

SUMMARY AND CONCLUSIONS.

The evidence available indicates that infected teeth elaborate two distinctly different products, one being bacteria, and the other a toxic substance or group of toxic substances, which, independently of the organisms developing them, may produce various and profound disturbances in tissues in various parts of the body, one of the important group of disturbances being that of the blood stream.

CHAPTER XXVI.

CHEMOTAXIS AS A MEANS FOR INCREASING DEFENSE.

PROBLEM: Can defense for streptococcal infections be increased by introducing enterally or parenterally (by ingesting or injecting) chemicals?

EXPERIMENTAL AND DISCUSSION

For hundreds of years the natives of Peru have been fighting malaria by chewing the bark of various species of cinchona trees containing the active principle of quinine. Modern science has perfected the process, and now injects into the circulation of the affected person, derivatives of that original compound, which are conceived of as having specific action on the plasmodium which produces malaria. This might be looked upon as true chemotaxis. Similarly, Ehrlick developed the administration of compounds of arsenic, known as "606" or salvarsan, which, under certain conditions, tends to be specific for treponema pallidum. Still later, compounds have been made of chaulmugra oil, which have very specific action in the treatment of leprosy. Similarly, Wright and others have used ethylhydrocupreinhydrochlorate in the treatment of pneumonia, particularly in epidemic form, which is disastrous in the mining districts of South Africa.

With a view to determining whether or not some such products enhance the defense of rabbits inoculated with cultures of dental origin, we have made several studies in order to determine more exactly the effect of the medication. We have studied the morphology of the blood before and after its use. The chart in Figure No. 158 shows the result of a series of inoculations made with ethylhydrocupreinhydrochlorate. The procedure of the experiment was as follows:

The rabbits of a group of eight were inoculated with decreasing doses of a culture which was grown from a tooth of a patient suffering from an acute eye involvement. This culture was selected because of its uniformly fatal termination with dilutions from one cubic centimeter to one-eighth of a cubic centimeter of culture. The rabbits of this group are shown in Section I of the

CHEMICAL MEANS FOR INCREASING DEFENSE.

Case No. 1131

R. No.	Chemical		Amount of Culture cc.	Method of Inoculation	Days Lived	Death	
	Amount cc.	Dilution				Sponta-neous	Chloro-form
Section I. Eight Control Rabbits.							
458			1.0	Intra-V	½	*	
461			1.0	Intra-V	1	*	
444			1.0	Intra-V	1	*	
447			1.0	Intra-V	1	*	
457			1.0	Intra-V	1	*	
465			0.5	Intra-V	1	*	
468			0.25	Intra-V	½	*	
469			0.125	Intra-V	3	*	
Section II. Rabbits Injected with Ethylhydrocupreinhydrochlorate before Culture.							
407	1/10	1%	1.0	Sub-C Intra-V	10	*	
427	1/10	1:5000		Sub-C	10		*
*428	1/10 1/10 1/10 1/10	1:1000 1:100 1:1000 1:5000	1.0	Sub-C Sub-C Sub-C Sub-C Intra-P	98		*
481	1	1:100	0.25	Intra-V Intra-V	30	*	
484	2	1%	0.5	Intra-V Intra-V	67		*
485	1	1%	0.5	Intra-P Intra-V	14	*	
486	2.5	1%	0.5	Intra-V Intra-V	78		*
Section III. Rabbits Injected with Ethylhydrocupreinhydrochlorate after Culture.							
482	1.0	1%	1.0	Intra-V Intra-V	1	*	
487	3.0	1%	0.5	Intra-V Intra-V	1	*	
512	1.5	1%	0.5	Intra-V Intra-V	1	*	
Section IV. Rabbits Injected with Culture and Ethylhydrocupreinhydrochlorate Simultaneously.							
490	3.0	1%	0.5	Intra-V	23	*	
510	2.5 1.0 1.0	1% 1% 1%	1.0	Intra-V Intra-V Intra-V	15+		

* Rabbit 428 received both chemicals.

FIGURE 158.

CHEMICAL MEANS FOR INCREASING DEFENSE

Case No. 1131

R. No.	Chemical		Amount of Culture cc.	Method of Inoculation	Days Lived	Death	
	Amount cc.	Dilution				Spontaneous	Chloroform
Section V. Rabbits Injected with Ethylhydrocupreinhydrochlorate Alone.							
521	1.0	1%		Intra-V	29		*
522	1.0	1%		Intra-V			
	1.0	1%		Intra-V			
	1.5	1%		Intra-V	54		*
Section VI. Rabbits Injected with Chaulmugra Oil Compound before Culture.							
488	2.0		0.5	Intra-P	70		*
492	1.0			Intra-P			
			0.5	Intra-V	45	*	
*428	1.0		1.0	Intra-P	79		*
Section VII. Rabbits Injected with Chaulmugra Oil Compound Alone.							
477	2 m.			Sub-C	28	*	
480	1 m.			Sub-C			
	1 m.			Sub-C	54		*
250	1 cc.			Intra-P			
	2 cc.			Intra-P	36		*

* Rabbit 428 received both chemicals.

FIGURE 158 CONTINUED.

chart, in which it will be seen that all of the rabbits died in from twelve hours to three days, all but one in one day or less. The rabbits which did not die during the work hours of the day on which they were inoculated, but were dead on the following day, were recorded as having lived one day. It is probable that several of them that are recorded as having lived one day, really lived much less than a day. The average, therefore, for the group would probably be pretty close to one day, which was too short a time for changes to take place that could be recorded as percentage loss in weight per day.

Section II shows a group of seven rabbits that were inoculated with the indicated quantities of ethylhydrocupreinhydrochlorate prior to their receiving the indicated quantities of the same culture as the rabbits in Section I, and it will be seen that most of these rabbits were still living in from one to two months, when they were chloroformed for tissue sectioning and study; and, whereas, one-eighth of a cubic centimeter of this culture sufficed

to kill without the assisting protection of ethylhydrocupreinhydrochlorate, those receiving it were enabled to withstand eight times that lethal dose for weeks or months.

In Section III we have a group of three rabbits that were injected with ethylhydrocupreinhydrochlorate after, instead of before, receiving the injection with the culture, and it will be seen that these rabbits all died spontaneously within a day. In other words, the administration of this chemical after the inoculation had had an opportunity to establish itself, failed to reinforce the defenses of the body sufficiently to stamp it out or to protect the animal from its ravages.

In Section IV we have two rabbits that were inoculated with the culture and ethylhydrocupreinhydrochlorate simultaneously, the first one of which lived twenty-three days, and the other was still in good condition in two weeks.

In Section V we have two rabbits that received ethylhydrocupreinhydrochlorate alone, and one of these was chloroformed in twenty-nine days and the other in fifty-four days, to ascertain the effect, if any, of the chemicals.

Section VI shows three rabbits that were injected with chaulmugra compounds before the culture, and it will be seen that the first one was chloroformed in seventy days, another died in forty-five days, another was chloroformed in seventy-nine days.

Section VII shows three rabbits that received the chaulmugra compounds alone without the culture. The first rabbit died spontaneously in twenty-eight days, the second was chloroformed in fifty-four days, and the third was chloroformed in thirty-six days.

From these data it will be apparent that these chemicals have shown evidence of reinforcing the defense of the rabbits against this culture which was taken from the infected tooth. The tooth itself was not giving the patient any trouble but was removed because of the fear of its having contributed to an optic neuritis which had completely destroyed the sight of this patient's eye. This culture, as previously stated, was used for this test because of its high virulence. There was, however, an unfortunate phase of the selection of this particular culture, which was that since there would be some reason to fear that it would have an affinity for eye tissues, since that was the serious lesion from which the patient had suffered, we might confuse elective localization qualities on the part of the organisms with elective localization

qualities of the defensive chemical injected. It so happens that one of these drugs—namely, ethylhydrocupreinhydrochlorate—has been suspected of producing injurious effects on the eyes of patients that were injected with it as a means of increasing their defense against the pneumococcus in cases of severe pneumonia. There is, however, a strongly expressed difference of opinion as to whether such injurious effects had been produced by this drug, or whether they were incidental or of other cause. In our rabbits inoculated with this culture, which was suspected to have had an elective localization for eye tissue, there was no opportunity for eye involvement to develop, since the animals were practically all dead inside of a day, only one living beyond that period, and it received an exceedingly small dose. Before this drug is used on humans as a means of reinforcing their defense against streptococcal infections, it is exceedingly important that extended researches be conducted to establish whether or not there is a danger of producing injuries to the eyes from its use. Several of the rabbits that received this drug prior to their injection with the culture, and which rabbits apparently had their lives lengthened or saved by the use of this chemical, developed conjunctivitis, and it was impossible to decide whether the lesion had been produced by the chemical or by the culture. Since, however, none of the controls which received the chemical without the culture, developed eye involvement, though they lived for from twenty-nine to fifty-four days before being chloroformed, it seems probable that the eye lesions which did develop, were the result of elective localization qualities on the part of the organism rather than the specific effect of this chemical.

With regard to the chaulmugra compounds, I found great difficulty in securing suitable extracts or compounds, and I found it necessary to engage the services of a skilled pharmacologist to make for me special preparations for my studies. A number of preliminary studies were made by using the chaulmugra oil and resorcin or camphor, but a special sodium chaulmugrate proved to be the least irritating and most efficient. A group of rabbits, not shown in our charts, received various dosages to determine the quantity that would be lethal and the quantity that would be most efficacious. This is presented as a preliminary report and more extended and detailed information will be reported later.

It will be noted that, of this group, many of the rabbits with-

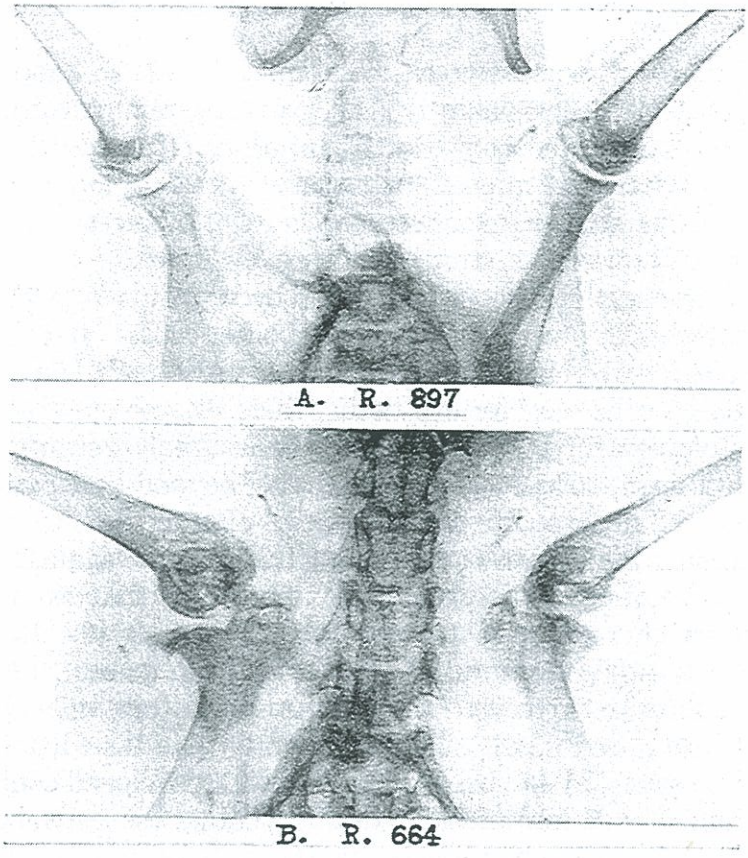


FIGURE 159. PROLIFERATIVE ARTHRITIS SHOWN IN SHOULDERS IN B. A, NORMAL; B, HAD RECEIVED LETHAL DOSES OF DENTAL INFECTION BUT HAD APPARENTLY SURVIVED BECAUSE OF THE RAISING OF ITS DEFENSE BY CHEMOTAXIS.

stood the lethal doses and lived on for long periods, and were used finally to see whether the use of chaulmugra oil continued to give them defense. Rabbit No. 664 had the following history: The rabbit received four injections on four successive days with a culture, one of which injections was expected to be sufficient to kill an ordinary rabbit. It had been prepared by a previous inoculation with sodium chaulmugrate. It gained splendidly in weight and looked like a very normal rabbit. Its fur was sleek; and when posted, it was very fat, notwithstanding all of which, multiple arthritis was found, as shown in the roentgenograms in Figure 159. The roentgenograms of the shoulder joints of a normal rabbit are shown for comparison in the same figure in A. This would seem to suggest that, notwithstanding this animal was not able to prevent the localization of the organisms having an

affinity for joints, it was able in large measure to resist the usual physical disturbances accompanying that process; for, notwithstanding its joints continually, though slowly, grew worse for six months, with a marked tissue change and accumulation of pus, it did not go into a state of decline with the characteristic decrease in weight which usually accompanies active rheumatic infection.

SUMMARY AND CONCLUSIONS.

There are several phases of this that must be kept in mind. First is the danger that may be done by injecting of such substances. This is particularly true of ethylhydrocupreinhydrochlorate, which may have a distinct injurious effect upon the eyes; and those who read this must be sure not to use it upon patients until much more work is done with it. The chaulmugra oil compound derivatives show promise of benefit. The experimental data are entirely inadequate as yet, however, to justify its use on patients.

These preliminary experiments would seem to suggest that, means can be developed which will effectually assist, by chemical means in the defense of the body against the invading streptococcal organisms of dental origin or from other sources which produce the rheumatic group lesions.

CHAPTER XXVII.

THE EFFECT OF RADIATION ON DENTAL PATHOLOGICAL LESIONS.

PROBLEM: Can periodontoclasia and apical abscess and inflammation be cured by various types of radiation?

EXPERIMENTAL AND DISCUSSION.

We began our studies on this problem in 1897 and 1898, immediately after the announcement of the discovery of the Roentgen-rays and the acquisition of our first apparatus, which was one of the first west of New York City. These were followed by studies with radium before the name, "radium," had been given to it, and when the material from which the radium was finally isolated was called "Radio-active substance". I published a preliminary report on the former in The Archives of Electrology and Radiology, March, 1904[1]; and on the latter in the Dental Cosmos, May, 1901[16], read before the International Dental Congress in Paris in 1900.

The early forms of apparatus for developing Roentgen-rays, used tubes that were very soft and which operated on a potential represented by a spark gap ranging from a half inch to two inches. Many of these tubes required relatively long exposures because such a small percentage of the ray had sufficient penetration to reach the film, which was the reason for our early researches on the development of the triple-coated film which, if I am correctly informed, was the origin of the original Seed film which was later taken over by the Eastman Co.

We early discovered that when teeth with fistulae were subjected to the radiations from these tubes, the fistulae tended to close; that sore teeth became less sore. One of these incidents was about as follows: The patient was sent by a fellow-dentist for a roentgenogram of a tooth with a fistula which the dentist advised should be treated. After our several exposures, taking different angles, the fistula closed and the man refused to pay for the roentgenograms on the ground that they were not needed, that the tooth had cured itself. We, accordingly, established a series of

investigations to determine what the effect might be on gingival infections as well as apical involvements when treated by this means. A series of special tubes with lead protectors was made to put into the mouth, generate the rays close to the tooth, and administer the dosage without raying other tissues. In our first group, we so treated a dozen and a half patients, about two-thirds of whom showed marked improvement when judged by the criteria of the flow of pus.

Enough data are available to demonstrate that we are dealing here with a force which, when it is understood, will doubtless be capable of lending great aid in the treatment of pathological conditions and, indeed, is already doing so in the treatment of neoplasms. We must, however, clearly distinguish between those changes from normal which develop in tissues as the clinical expression of the pathological involvement. In some instances we have a very markedly lowered capacity for reaction to irritation. Invaded tissues do not have the capacity for defending themselves against the parasitic intruder. Their very lack of vital reaction determines the outcome of the warfare immediately at the outset, for the condition must go from bad to worse, the organism gaining more and more vitality and virulence, as the tissue develops less and less capacity for defense. Clearly what this tissue needs is something that will boost and support its already too feeble capacity for reaction. This we will discuss presently. Over against this we have another type of reaction in tissue, in which the pathological state expresses itself with abundant cell proliferation and more than normal reactions, which process will include the neoplasms such as the various cancer growths and some stages of periodontoclasia, or pyorrhea alveolaris.

When radium, then, is applied to a neoplasm such as an epithelioma, it depresses that vital capacity which expresses itself in cell proliferation, and, if the dosage is properly adjusted, this depression may be sufficient to restore this tissue approximately to normal, by destroying or depressing all cells having that exalted capacity. If, however, this same type of cell depressant is applied to tissue whose only safety lies in its capacity to exalt its activity to any needed extent to baffle and overcome the invading infection, it is like putting the brakes on a wagon which the overloaded horse is struggling with his most extreme effort to take over the grade. In other words, those forms of radiation, which

tend definitely to depress vital function, must not be used to depress function where an exalted function is desirable.

The type of bacterial flora present in a periodontoclasia pocket will indicate very directly and definitely many qualities of the environment from which it is taken. To the trained eye familiar with the microscope the bacterial culture reveals very definitely the type of inflammatory process present. One of the greatest mistakes that has been made in the study of suppurative periodontoclasia, or pyorrhea alveolaris, has been to interpret the cessation of the development of so-called pus as a cure of the lesion; and this is one of the mistakes that I made in interpreting the clinical results produced by my treatment of cases of so-called pyorrhea alveolaris twenty years ago, as reported in The Archives of Electrology and Radiology, March, 1904 (The Treatment of Pyorrhea Alveolaris with the X-rays.). I mistook a depression of the tissues, as expressed by their capacity to produce an exudate, as a cure. There is no doubt that some of the conditions were definitely benefited, and others were definitely aggravated, by that same treatment, for they represented entirely different stages of a pathological process, one hyperactive cell reaction, in which cases were benefited, and the other, a chronic depressed reaction state, in which cases were, doubtless, not only not improved, but, probably, definitely injured.

To test this further, I have made a series of studies with the mercury vapor arc lamp, to determine its effect upon the clinical conditions, as interpreted in the light of our newer knowledge, with the result, that there seemed definite evidence of a depressing effect on cell reaction, which was beneficial in only those cases having an exalted reaction state, and was definitely harmful in those cases with a depressed reaction state. To test this further, we placed teeth under the skins of rabbits and exposed the tissue over the implanted tooth to the quartz mercury vapor lamp. In every instance the animals died more quickly with this treatment plus the infected tooth, than with the same infected tooth without the mercury vapor lamp radiation; and, furthermore, we found that, whereas, when the rabbits died from the presence of the infected tooth alone, there was found all about the tooth an exudate carrying an abundant quantity of leucocytes; but when the rabbit was exposed to the radiation for fifteen minutes a day as we had been exposing our patients, there was found about the tooth practically a pure culture of streptococci

with exceedingly few leucocytes; and, furthermore, when rabbits were exposed to the radiation without the presence of the infected tooth, we found that the radiation produced a definite depression of the leucocytes of the blood.

These studies strongly urge the establishment of researches which will adequately determine, first the reaction effects of the rays of various angstrom units, and second, a very careful differentiation between an exalted and a depressed cell activity in the various pathological states with which we are concerned. It would seem most unwise that routine clinical application should be undertaken before these fundamental problems shall be worked out. Some phases of this question will be discussed in the next chapter.

I have undertaken to apply rays of an angstrom unit between 300 and 1200 from mercury vapor arc in the treatment of periodontoclasia. One of the cases selected is shown roentgenographically in Figure 160. This was a case of chronic periodontoclasia, with much destruction of tissue and loosening of the teeth. The method of determining the presence or absence of improvement was by testing the hydrogen-ion concentration of the saliva, the bacterial types, and the quantity of their growth in the pockets, and the tightening of the teeth, with the improvement in the ap-

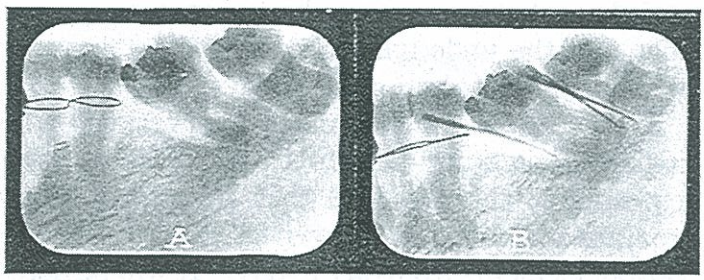


FIGURE 160. A CASE OF PERIODONTOCLASIA TREATED WITH ULTRAVIOLET RAYS FROM A QUARTZ MERCURY VAPOR ARC. A, IS WITHOUT GUTTA-PERCHA POINTS IN POCKETS, AND B WITH. NOTE HOW DECEIVING A IS.

pearance of the gingival tissue. As judged by these criteria, there was but slight, if any, improvement; and, particularly, when judged by the bacterial flora, which is one of the best indications. In the second view in B, flexible gutta-percha points are placed in the pockets between the teeth; and the advantage of their use is very apparent, for it will be noted that in A the pocket between the two molars does not appear to be nearly as deep as it is shown to be by the passage of the flexible points, which stresses

what so many have learned to their chagrin, that the conditions were very much worse than they were supposed to be, when judged simply by the roentgenogram. The dosage given was fifteen minutes with a quartz applicator, twice a week, for about ten weeks. If improvement would not be produced in that time, the treatment would not justify its continuance in our judgment. The slight improvement in the types of bacterial flora was temporary and tended to return to its former type quite early after the cessation of the treatment.

In order to determine more exactly what the effect of such treatment would be, I placed an infected tooth beneath the skin of a rabbit, and treated same with the quartz mercury vapor arc lamp by flooding the tissues over where the tooth was planted beneath the skin, with these rays for fifteen minutes a day for two days, the day of the implantation and the day following. On the third day it was chloroformed. It was our belief that the tissue broke down more rapidly, and tissues became a prey to the infection more speedily, than when this tooth and other teeth were planted beneath the skins of other rabbits. There was also a very marked decrease in the number of leucocytes present in the fluid surrounding the infected tooth. The rabbit was posted on the third day, at which time it had lost 130 grams, or 10 per cent, and showed at necropsy, subcutaneous gangrenous necrosis, with edema of the underlying tissues. There was marked hyperemia of the thyroid, spleen, and kidneys.

I, therefore, decided to make observations on the effect of these radiations on a normal rabbit. Its blood was studied prior to its exposure to the rays and then frequently observed during the treatment. Results are shown in Figure 161, which records the various elements from day to day. It will be noted that there was

EFFECT OF RADIATIONS ON BLOOD OF NORMAL RABBIT

Date	Hemoglobin	Erythrocytes	Leucocytes	Polynuclears	Lymphocytes		Basophiles	Mononuclears
					Large	Small		
*3– 8–23	85	7,000,000	7,200	**59**	8	**24**	1	8
*3– 9–23	85	4,300,000	10,800	**64**	16	**17**		3
3–10–23	85	4,550,000	7,800	**53**	12	**26**	2	7
3–12–23	80	4,770,000	4,600	**40**	11	**43**	2	4
*3–14–23	85	5,150,000	6,000	**36**	8	**55**		1
*3–15–23	85	5,650,000	9,900	**35**	8	**54**	1	2
*3–19–23	80	5,800,000	5,400	**43**	6	**50**		1
3–23–23	80	5,050,000	7,800	**41**	11	**46**	2	

* The rabbit received 15 minute treatments following the blood counts

FIGURE 161.

a decrease in the percentage of polymorphonuclear cells, with a marked increase in the small lymphocytes. In our studies with infected teeth planted beneath the skins of rabbits, and when cultures are inoculated of dental origin, there often develops a decrease in polymorphonuclears and an increase of lymphocytes as part of a developing leucopenia, which depression of leucocytes always indicates a poor defense progressing toward death, which usually cuts short the experiment in a few days after its development. A very important effect of the radiation on this rabbit is expressed in the change in ionic calcium of the blood, as shown in Figure 162. On the 8th, this was 10.4 mgs. per 100 cc., approximately normal. The first reaction to the stimulation of a single exposure increased the ionic calcium to 11.13; and on the 13th, this had changed to a distinct pathological state of 8.27. Another very striking feature of this change relates directly to calcium metabolism; for the combined calcium of the blood on the 8th was 1.7; on the 9th, it had increased to 3.7; and on the 13th, to .5.

EFFECT OF RADIATIONS ON BLOOD CALCIUM OF NORMAL RABBIT

Date	Calcium plus Thrombin	Thrombin Equivalent	Calcium Ionic	Calcium plus Combined	Combined Calcium
3– 8–23	17.60	7.199	**10.401**	12.13	1.729
3– 9–23	19.00	7.866	**11.134**	14.878	3.744
3–13–23	17.20	8.923	**8.277**	8.793	.516

FIGURE 162.

I have made a number of studies with radium, and have found it very difficult to be sure that I was properly interpreting the results because of the difficulty of knowing the proper dosage, for just as a little strychnine may be good, and a very little more may be very harmful, just so a proper dosage of radium or otherwise, may be distinctly beneficial, and just a little more distinctly harmful. I am, therefore, withholding these studies until I have more data, for it is exceedingly difficult properly to control and limit the effects of radiation to the pathological tissue, it being so intimately related, anatomically, to normal tissue; and the very treatment which may be a benefit to the former, may, at the same time, be harmful to the latter. If we put a medication into a pocket of periodontoclasia, its action may be quite completely limited to the tissues with which it comes in contact and those very closely adjacent. Radiations, on the contrary, pass not

only through the adjacent tissue, but through the entire body in many instances, and the dosage and application are not within easy control. For this reason we have undertaken to use the radiations from silver chloride in colloidal suspension but, while these have bactericidal effects, and will even pass through a glass tube, we have not found that placing either the tooth containing a tube of this material, or the tooth saturated with it, was sufficiently less harmful, when planted beneath the skin, to assure us that it was an efficient germicide. It is a favorable field, however, for investigation.

There are many reasons to believe that great benefit will ultimately come from an adequately intelligent use of radiations of various lengths, when properly selected and adapted to the needs required. We now know that neoplasms represent a diverted cell function, which, in the proliferative types, express an overactive state; and any force which tends to depress, will thereby suppress the proliferation. For this the very short rays of the x-ray and radium tube are most efficient. Similarly, we know that radiations of the range of three hundred to six hundred tend to produce beneficial changes in rickety conditions; and again, we know that whereas animals will die of vitamin deficiency when fed on dried peas, for example, they will be promptly restored by being fed on these same dried peas that have been allowed to sprout and been exposed to sunlight. Similarly, the algae of the sea, through their exposure to the sun's rays, have become immense storehouses for vitamins, which latter are stored in the livers of the fish, and hence are largely in use, medicinally, in cod liver oil. It is also general knowledge that sunlight is necessary for health. The rickety children in a smoky city will recover by being moved to the sunlight of the clear country, even though retained on the same diet. Not only is this true, but just as the distance from the equator is lengthened, mankind is required to use more of the vitamin storage foods as he approaches the shorter days and hence decreased sunlight, which is the reason that Labradorians and Arctic inhabitants live so much on the fats and oils of fish.

When we come to know the true nature of disfunctions of various tissues and organs, we can then judge wisely what type of ray should be used to improve its condition, and interpret wisely what constitutes an improvement and what an apparent improvement but an actual injury. An illustration of the latter can clearly be seen in the misconception regarding the significance of a closing of

a dental fistula after exposure to Roentgen-ray, and the cessation of the so-called pus from periodontoclasia from exposure to Roentgen-ray and other radiations. I am not decrying these means, but I am trying to point out that we must understand their fundamental pathology before we can treat them intelligently or interpret wisely the results of our efforts. This, therefore, is a field that represents a crying need for exhaustive research on the basis that will be competent to bring about dependable and properly interpreted results.

CONCLUSIONS

The results of these studies suggest to me the following:

(1.) That these three forms of radiation—namely, Roentgen-ray, radium radiation, and ultraviolet as generated from mercury vapor and quartz tube—have definite effect on cell resistance to proliferation, and thus directly upon tissue reaction expressions such as pus, bacterial invasion, and granulation.

(2.) That some of these forces are, apparently, definitely harmful; that others are, apparently, definitely helpful.

Our interpretations of these phenomena are given in Chapters 45 to 56.

CHAPTER XXVIII.

GINGIVAL INFECTIONS, THEIR PATHOLOGY AND SIGNIFICANCE.

PROBLEM: Are the present theories regarding the etiology of periodontoclasia, or so-called pyorrhea alveolaris, correct?

EXPERIMENTAL AND DISCUSSION.

I cannot find in all of medicine, whether in general medicine or in the specialties including that of dental medicine, instances of very common diseases which have so completely baffled explanation or which contain so many paradoxes as has this disease. In the minds of the majority of the members of the dental and medical professions, and as well, and naturally so, in the minds of the members of the laity, this disease is thought of largely as a true infection process. The imperative necessity for brevity in these reports precludes the possibility of presenting, herewith, a history of the theories as to its etiology. For such, I would refer to various books on general or dental pathology.

Lately, it has come to be recognized and thought that irritants play an important part, and that their removal becomes a fundamental part of the treatment of this disease, though their removal does not explain its etiology. Similarly, traumatic occlusion has come to be recognized as an irritant and, like a foreign substance, must be corrected. One of the advanced thinkers in the etiology of this disease, Eugene Talbot, has advocated that the supporting structures of the teeth are transient tissues and, as such, tend readily to be absorbed, which accounts for the fact that, in the presence of bacterial invasion and irritation, that process which is part of senility, sets in early. In his paper entitled "The Etiology and Treatment of Interstitial Gingivitis,"[16] he states:

"When we consider the peculiar endotransitory nature of the alveolar process, degeneration of tissue is the natural result. At the senile period when the excretory organs are diminishing in

[16] See bibliography.

activity and in disease, vital resistance is at its lowest ebb, metabolism is diminished, and degeneration and absorption of the alveolar process is in active operation. As age advances, the destruction of bone is a natural normal pathologic process".

About twenty-five years ago, I started a quite intensive study of this disease, and found that every time I approached the problem through the doorways of the available theories, I ran into a network of contradictions and confusions which persuaded me that there were some things fundamental, of which we were not as yet appraised, and which were the most important factors in the etiology of this disease. And since the workers in this field had apparently not succeeded by approaching from the regulation doorways, I decided to make a new approach—namely, by way of an exhaustive analysis of the clinical data and a careful examination of the characteristics of the individuals presenting with that affection, and relating these data to the blood and saliva chemistry and bacteriology. Accordingly, as a part of the susceptibility study to streptococcal infections, we have carried on an extensive study of the characteristics of all individuals with regard to their susceptibility to gingival and alveolar infections. There soon appeared in these studies, either a great anomaly or a great truth. For a long time we could not accept it as a fundamental truth; it was so paradoxical to the conception we had entertained.

In discussing the clinical phase of this group of affections, I have presented much data which are necessary for our approach here, and to save repetition, I will refer back to those chapters for many references These are found particularly in Chapters 4, 8, and 10.

Figure No. 44 shows the result of a series of studies that was made several years ago, and tabulated three years ago, which showed that, when patients with or without susceptibility to rheumatic group lesions, were divided into progressive groups in accordance with the degree of that susceptibility, a very important change took place with regard to their susceptibility to periodontoclasia. In Group No. 1, absent susceptibility, the percentage with periodontoclasia was 23; Group No. 2, acquired susceptibility, 33%; Group No. 3, very mildly inherited susceptibility, 25%; Group No. 4, moderately strong inherited susceptibility, 0%; and Group No. 5, very strong inherited susceptibility, 0%;whereas, in these various groups extensive caries was

as follows: Absent susceptibility, 51%; acquired susceptibility, 91%; mild inherited susceptibility, 81%; moderately strong inherited susceptibility, 88%; and very strong inherited susceptibility, 100%; and the presence of locked dental infection tended to increase from 58% absent susceptibility, 75% acquired susceptibility, 44% mildly inherited susceptibility, 75% moderately strongly inherited susceptibility, to 86% very strongly inherited susceptibility.

In order that we might thoroughly check so great a new truth, if such it be, before presenting it, and with the most earnest desire not to permit an error to be presented, we have refrained for several years from announcing this important discovery, awaiting a satisfactory mass of data that would either establish or disprove it. Accordingly, a new corps of assistants has tabulated a new group of findings, not knowing either the results of the former studies in this regard, or even that they had been made. These results are shown in Figure 85 of Chapter 10, the latter chart giving as follows: Absent susceptibility 40; acquired 33; inherited one side mild 33; two sides mild 20; one side strong 20; two sides strong 0.

This was further shown in Figure 87 which reveals that, when individuals are divided into three groups—absent, acquired, and inherited (the latter of all grades of inheritance)—, the percentage of individuals affected with periodontoclasia in the group recorded as absent susceptibility was 48; acquired susceptibility 29; and inherited susceptibility 16.

All observing dental clinicians have noted for decades that teeth with extensive gingival infection do not suffer carious destruction. This paradox seems to hold an important key to the interpretation of much of dental pathology.

An extensive study of the bacterial flora found in periodontoclasia infections has demonstrated that there has been a great divergence of opinion as to the causative invading organisms. Of the workers, Hartzell and Hendersy have stressed the importance of streptococci, while most workers, both early and late, have noted the presence of spirochetes and fusiform. The great drawback in the study of this disease has been found in the fact that the characteristic bacterial growth cannot be produced in artificial media. Some of the workers have been able to grow a few of the organisms. Our studies have shown a quite definite tendency to grouping of bacterial types of infection: those in

which fusiform and spirochæte abound almost exclusively; those in which spirochæte abound almostly exclusively; and those where these two types are very scarce, if not almost entirely absent, with an abundance of short rods, staphylococci, streptococci.

In order to determine the significance of the important data revealed in the relationships between gingival infections and the other outstanding clinical conditions—namely, presence or absence of dental caries, presence or absence of systemic involvement, types of local dental pathology—we have related each of these conditions as found in various individuals to the serological and chemical changes in the blood, saliva, urine, etc., of those individuals.

In Figure 85, Chapter 10, I have shown that tendency to gingival infection is, in large measure, in proportion to defensive activity, and, therefore, in proportion to absence of rheumatic group lesions, these figures progressing from 40 per cent of the individuals with absent susceptibility having periodontoclasial processes, 33 per cent of the acquired group, 33 per cent inherited one side mild, 20 per cent inherited two sides mild, 20 per cent inherited one side strong, and 0 per cent inherited two sides strong. I do not present these figures with any thought that they are exact, but, when taken from such a large number of cases and from several groups by different individuals, the fact that the result is, in general, constant, suggests that they are relatively correct. We do not yet know the significance of many of the new data that we are here presenting, but it is a matter of exceeding interest and of undoubted importance, that patients with active periodontoclasia without exception, in our experience, have been found to have a high ionic calcium, in the order of 11 to 12.5 mgs. per 100 cc. of blood, as compared with 10 to 10.5 for our accepted normals.

An analysis of this clinical data reveals the remarkable fact that in some way the presence of an active defense against streptococcal infections, in so far as the absence of rheumatic group lesions is concerned, is directly related to the clinical expression which we find as periodontoclasia, or pyorrhea alveolaris, *in certain of its stages*. It is not an accident that so many people with such extensive gingival suppurative processes are apparently in excellent health.

For determining the factors involved in the lesion known as periodontoclasia, or pyorrhea alveolaris, we have undertaken to

discover the contributing influence of each. An analysis of these suggests that mechanical irritation, bacterial invasion, and defensive reaction, all play important parts. In order to determine the relative importance of all of these we have treated different groups in different ways. In the first group no other means has been used than the mechanical removal of irritation; in the second group no other means than local bactericidal treatment; in the third group systemic bactericidal treatment; in the fourth group the changes in the peridental tissues where the individual's defense had been lowered by inflammatory and other causes; the fifth group artificial stimulation of gingival tissues. These showed as follows: That in the early stages of periodontoclasia the simple elimination of the substances producing mechanical irritation, thus removing the primary irritant which caused the inflammatory reaction, entirely removed the periodontoclasia, or pyorrhea alveolaris. In the far advanced conditions the removal of the mechanical irritant made much less improvement, and in some cases very little. In the series of cases studied to show the effect of local bactericidal treatment we have many illustrations which reveal a marked improvement in the clinical conditions with no other treatment. The effect of systemic bactericidal treatment, in which case the injection of emetin and succinimid of mercury was used, showed marked improvement in local clinical symptoms even though the mechanical irritant was not disturbed.

Another series of studies was very illuminating. These were conducted in 1898 to 1904 on the use of the Roentgen-ray in the treatment of periodontoclasia, which we have discussed in the preceding chapter and which was published in The Archives of Electrology and Radiology, March, 1904.[1] In those studies I found that Roentgen radiations tended to depress the reaction capacity of the tissue to a marked extent.

Inasmuch as the local bactericidal treatment and the mechanical removal of the irritants each produced practically complete removal of the local oral symptoms, it suggested very strongly the great need for a research upon the problem of the improvement of germicidal procedure. For this purpose a series of researches has been carried on for several years, at one time taking practically the entire time of a trained bacteriologist for one year, to ascertain the drugs and chemicals that were most efficient in depressing the type of bacterial growth which tends to develop

[1] See bibliography.

in the mouth, in which there is a marked susceptibility to development of periodontoclasia, or pyorrhea alveolaris. These researches themselves would fill a volume and will only be summarized here to present the important results. Their application is made in extended detail in a later presentation.

The following types of drugs were found most efficient, though some were not suitable because of undesirable qualities: Mercuric nitrate (This discolors the teeth in time and has the possibility of systemic irritation.); chaulmugra compounds; chlorine compounds; zinc compounds, particularly the chloride and sulphocarbolate; silver compounds.

In the group of individuals studied by mechanical stimulation of gingival tissues, a very marked change in the local clinical conditions was shown. With the improvement of the circulation, there was a marked decrease in both the bacterial growth and development of exudate and also in the hypertrophy and congestion, notwithstanding the fact that the massage was done against tissues, which were being pressed against rough deposits on the necks of the teeth, the effect of which was to lacerate and injure these tissues. Notwithstanding this latter fact, the improvement was very marked.

Since it is demonstrated that marked beneficial results may be secured by each and all of the methods of procedure, though some more than others, it becomes apparent that the utilization of those means, which are most easily applied, will in many cases be all that is necessary to prevent the development of this clinical condition. This involves first the mechanical removal of irritation; second, the use of bactericidal means for depressing the type of organisms which develop in this condition; third, the use of mechanical stimulation to prevent the passage of those fluids which tend to nourish the bacteria from the surrounding tissue into the pockets of periodontoclasia and to provide the rapid exchange of fluid in the involved vascularized tissues in order to bring new defensive factors and carry away waste products, the use of substances producing radiation in order to reduce to normal the reaction capacity of the tissue exalted as a part of the infective process.

In the chapters on Tooth Medication, Radiation, and Chemotaxis, I have reviewed the effects of the use of substances producing radiation for reducing bacterial growth and exalted tissue reaction. In a later presentation I will give special formulas for

the development of tooth powders and methods for their use, suited to each of the different types of extreme oral conditions, such as tendency to caries, tendency to gingivitis, periodontoclasia, pyorrhea alveolaris, etc. These are so simple that they may be put up by any good druggist and should be available to humanity at small cost; and if used sufficiently intelligently and faithfully as indicated, will almost completely prevent the development of the disease known as periodontoclasia or pyorrhea alveolaris.

It is most important that we urge the reader to keep in mind a very great difference in the type of gingival infection which is typical of the active suppurative type in its early stages, which responds readily to the removal of local irritants and to stimulation, from the chronic non-suppurative poorly reacting condition. In this discussion we are referring distinctly to the early active process which has an entirely different pathology from the other types which represent the ravages of the former active processes, carrying it over into a changed systemic condition.

When we relate the following factors—namely, the relative extent of absorption of supporting structures, whether apical or gingival, the presence or absence of systemic involvements, the absence or presence of dental caries, the ionic calcium of the blood, the ionic calcium of the saliva, the alkali reserve of the blood, the alkali reserve of the saliva, the uric acid content of the saliva, the uric acid content of the blood, urea nitrogen of the saliva, urea nitrogen of the blood,—we find certain groups of conditions are, practically, invariably associated. The individual with the high defense has a normal ionic calcium of both blood and saliva. It is apparent, then, that this quality of the presence or absence of gingival infection with a given irritant is related directly to calcium metabolism. When we make a careful study of the characteristics of the various physical states which modify calcium metabolism most, we find that just in proportion as that individual is able to maintain a high or abnormally high ionic calcium balance of the blood, in that same proportion his gingival supporting tissues tend to be absorbed easily in the presence of irritation.

This research has been planned to establish, if possible, what some of the direct variable factors are in connection with this susceptibility to destruction of the alveolar bone in these cases. A careful study of the saliva reveals, and that readily, that it is

more alkaline in individuals with a marked tendency to periodontoclasia. A more exact study of the hydrogen ion concentration of the contents of the pockets of periodontoclasia shows that in the active condition it is very alkaline, reaching as high as 7.7 whereas the hydrogen ion concentration of the blood is 7.3.

In another chapter we have noted the important clinical fact that the sockets of extracted teeth, which teeth were involved with acute periodontoclasia, tend to heal with great ease and rapidity, seldom requiring a treatment following the extraction. A blood clot is readily formed. It is well organized. It becomes vascularized by the development of embryonic blood vessels in the clot, and its socket heals without pain and without the clot's ever breaking down; whereas, on the other hand, a socket of a tooth with marked condensing osteitis without a tendency to involvement tends to have its blood clot break down, readily becomes painful, and in many cases develops what is clinically termed "dry socket", which condition is characteristic. An analysis of the saliva of this type of patient shows a lower degree of alkali reserve; his blood shows a lower ionic calcium; and, immediately, we are dealing with two distinct types of individuals. This problem of the postoperative treatment of the sockets of various types of individuals will be discussed in a later presentation.

A careful microscopic examination of the contents of these two different types of sockets has revealed an important new group of facts, which are so constant, that they become immediately definitely diagnostic. The leucocyte found in the socket of the tooth extracted with periodontoclasia is largely a polymorphonuclear with several lobes. The cytoplasm is filled with granules which are readily disclosed either by the dark field or direct illumination, and with certain types of vital stains; but most important, these polymorphonuclears show a rapid motility of these granules. Many of these cells contain bacteria which are in relatively small quantities outside the leucocyte, in proportion to the clinical picture found in the other type of socket, which latter, in contrast to the former, has few leucocytes with actively motile granules, relatively few phagocyting leucocytes, and larger numbers of organisms outside these cells.

We have, then, a direct measure in this process of the activity, and since a socket shows, under treatment, these highly active granular polymorphonuclears, it usually goes on readily and rapidly to complete healing process. So far as we know, this

phenomenon has never been reported. We have not been able to find a reference to it in any literature or by correspondence with our leading hematologists.

A closer study reveals that, if in a socket of the second type—namely, without the presence of this large number of characteristic granular leucocytes whose granules are highly motile—we place an ionic calcium, as, for example, calcium chloride together with bicarbonate of soda, within a few hours the pain subsides, the type of leucocyte changes, and the type of socket has been changed so that it starts immediately on the process of repair. This has led us to a careful analysis of the relationship between the process of decalcification and ionic concentration of calcium, and these in relation to the alkali reserve of the blood.

A further analysis of the various charts in which we have compared the clinical expressions, structural changes, and chemical analyses, we find that in those cases where the suppurative process was most active, the content of the pockets of periodontoclasia were most alkaline, the ionic calcium of the blood high normal or above normal, blood sugar higher than normal, trabecular differentiation of alveolar bone very marked, caries low or zero, tissue repairing qualities excellent, inflammatory response to mechanical irritation acute, etc., all existing in an individual with every evidence of a high defense to rheumatic group lesions such as complete absence of heart involvement and rheumatism. In sharp contrast to the preceding, we find that the individual who has a marked susceptibility to rheumatic group lesions strongly tends not to have pockets of periodontoclasia even in the presence of irritation sufficient to produce same, such as gold crowns, food packs, etc. In him the ionic calcium of the blood is below normal, blood sugar not above normal, trabecular differentiation diffuse and not marked, caries high, tissue repairing qualities—particularly of alveolar bone—poor, inflammatory response to mechanical irritation subacute or low, etc.

This relationship between the clinical, serological, and chemical factors, has suggested to me that these must be related as cause and effect; and, accordingly, a series of researches is being made to ascertain, if possible, the mechanism of this reaction. We are, accordingly, taking a large group of extreme cases of each of the different types and carrying out these studies in further detail with especial reference to the relationships between the alkali reserve of the blood and the clinical symptoms, such as the

destruction of the gingivæ, the peridental membrane, and the alveolar bone.

From these data it is shown that as the alkali reserve goes down and the ionic calcium goes up, there is a marked tendency to acute inflammatory reaction to irritations, with necrosis of soft tissues, and absorption of alveolar bone; and where the alkali reserve is not below normal and the ionic calcium not up to normal, there is not marked reaction to irritation of gingival tissues and but little absorption of alveolar bone. In Chapter 44 I have discussed the relationships involved in these phenomena in detail. It is there shown that one of the system's most difficult and exacting operations is the maintenance of the normal hydrogen ion potential of the blood, which is made possible only by an ample reserve of buffers to take care of sudden increases in acidity or alkalinity, particularly the former, called the alkali reserve of the blood. For ordinary purposes in normal individuals this can readily be done by drawing upon the compounds within the blood itself together with respiration. This becomes increasingly difficult as that alkali reserve is reduced; and since the mechanism of defense is made very active, doubtless by hormones, but also very largely by a high ionic calcium of the blood, catabolic and physiologic processes are carried out with great ease and rapidity. For the process of defense against infection, Nature has provided the flooding of the parts with an alkaline plasma. The mechanism is available to create the alkalinity of the fluids bathing the parts in periodontoclasia, but the reserve supply of buffers is so greatly reduced, that Nature must resort to other sources of material for producing this alkaline medium. She, accordingly, must have some means for producing an alkaline medium in the absence of a low alkali reserve in the blood. In order to determine this reaction we have carried out the following research:

Since the hydroxyl ion is increased in the saliva of individuals with a marked susceptibility to periodontoclasia, it should be possible to determine what substances have taken part in that process by comparing the concentration of the various constituents in pockets of periodontoclasia and in the saliva itself, the latter furnishing the medium surrounding the environment, the former a mixture of the latter with the products of the reaction within the pocket. To determine this I have made a series of studies in which we have compared the following elements in the

pockets of periodontoclasia and in the mixed saliva of the mouth and compared them with the blood chemistry. Since the blood and saliva must largely furnish the constituents for the pocket of periodontoclasia, it immediately becomes apparent that any marked increase in any element found in the pocket of periodontoclasia over that of the blood and saliva will indicate that there has been some other source. These have shown that the total calcium of the pocket of periodontoclasia is much in excess of that of either the blood or saliva. This cannot be accounted for on the basis of concentration. It will be noted that as the OH ion increases in the production of alkalinity, there is an increase in the excess of calcium over that of either the saliva or blood. There is also an increase in the phosphorus. This immediately suggests the question, Where do these substances come from to make this excess? When we compare the relationship between the calcium and phosphorus of the saliva with those elements in the blood of individuals without periodontoclasia, we find that it is not normal for those substances to appear in the saliva in greater concentration than their existence in the blood, and that their concentration increases as the clinical expression of periodontoclasia. It is, therefore, apparent that this alkalinity is accomplished by an increased cell activity with an osteolysis partly the result of the increased concentration of calcium ions, which activity has torn down the alveolar structure to secure neutral calcium phosphate in the absence of the normal alkali buffers of the blood, whose normal function would be to supply this demand.

It frequently occurs that patients with profuse spirochete infections, are suffering from marked toxemia, with progressive loss of weight. A typical illustration of such a case is shown in Figure 186 of Chapter 35. This patient had lost eighteen pounds in weight in three weeks; and immediately following the treatment of his gums, the patient gained ten pounds in two weeks.

Since the preceding researches on the etiology of periodontoclasia, or so-called pyorrhea alveolaris, have demonstrated the important role of each alkali reserve of the blood, alkali reserve of the saliva, ionic calcium of the blood and ionic calcium of the saliva, it is important to determine, if possible, some of the mechanisms of the contributing factors to this process. Our microscopic studies referred to have revealed the presence of large numbers of a type of polymorphonuclear containing very actively motile granules. This leucocyte is also very abundant in the

sockets of extracted teeth which are repairing rapidly and satisfactorily, but greatly diminished or absent in sockets healing slowly or with pain or necrosis of tissue. As stated previously, it seems certain that these cells play a very important part, since they are present in both these conditions which represent in a sense opposing states, for one is rapid repair and building up of tissue, and the other is the tearing down of tissue. The same socket, from which the tooth with periodontoclasia is removed without any treatment whatever, practically always heals with exceeding rapidity and practically always without pain, necrosis, or infection. The placing of a foreign irritant, such as a piece of metal, in this same tissue does not produce the same type of reaction, either as expressed in exudate or tissue change, as does the presence of this type of tooth, mere removal of which completely reverses, or at least modifies, cell activity.

Normal adult tissue does not tend to proliferate after an organ or structure has reached its normal size. During the growing period, all tissues tend to multiply at a physiological rate constituting growth, which process is progressively slower with age until the adult development is reached. It is as though an arrow were shot from a bow, or a bullet fired from a gun. Each has its maximum velocity at the beginning of the flight. The velocity slackens at a definite rate; the period of rest is reached. In normal tissues there is no tendency to take up the condition of proliferation until conditions become abnormal. If tissue be injured, there is an immediate reaction in the local circulation, the capillaries distend, leucocytes come to the parts in large numbers, plasma exudes, and in proportion to the extent of the injury the reaction may include the entire body of the organism. White connective tissue cells rapidly begin to multiply; embryonic blood vessels extend from the capillaries; and after a clot has been formed and is not infected, this vascularization and rapid tissue generation extends into and throughout the clot. Finally, the tissues are rebuilt, proliferation ceases, rapidly formed connective tissue will be slowly rebuilt with the normal type of tissue of the part, and again Nature settles down to her normal, and there is no more cell proliferation.

This same process takes place when a tooth is extracted from a normal individual and is precisely the procedure with the repair of the socket after the extraction of the tooth. This, however, does not occur in those individuals with a low calcium and with a

marked susceptibility to rheumatic group disturbances. This is doubtless partly occasioned by the fact that, the tissue, which has to take part in the repair, is distinctly different in the two types of individuals. In those with high defense there is little sclerosed bone, the medullary spaces between the trabeculæ are normal in size, and the alveolar bone is well vascularized. We have shown from our clinical studies that, one of the most conspicuous differences between these two types in their healing process, is in the absence in the latter, and the presence in the former, of a particular type of leucocyte, a polymorphonuclear with highly motile granules.

SUMMARY AND CONCLUSIONS.

From these data we are led to conclude: First, that the fundamental factor in periodontoclasia, or pyorrhea alveolaris, is not a specific infection; second, its etiology is in a direct way related to the presence or absence of susceptibility, by both being symptoms of a definite systemic condition; and third, the disease we have known as periodontoclasia, or pyorrhea alveolaris, is in some very definite way related to defensive factors. Since all of these researches combine together to furnish the new interpretation, it becomes necessary to reserve that interpretation for the chapters assigned to that important part of this presentation. It will be found in Chapters 45 to 56.

We would briefly summarize our interpretation of these data as follows:

(1) Inflammatory processes of the tissues about the teeth are a direct expression, and therefore a measure of the vital capacity for reaction of that individual to an irritant, during those stages of these lesions, characterized by an abnormally high vital reaction.

(2) The individual, who has had this capacity for a very active reaction to the presence of irritants, may pass into a condition or state in which he or she has lost that high defensive factor, at which time several changes develop including a cessation of the absorption of alveolar bone, a lowering of the alkalinity of the periodontoclasia pockets, a change in their bacterial flora, all of which may provide under these later conditions a focus for systemic infection of the most danger-

ous type, though they may have ceased either to have evidence of local inflammatory disturbance, or exudate as pus.

(3) To the ordinary observer, lay or professional, these two very dissimilar states are considered to be similar or identical though they are potentially very different.

(4) These different peridental expressions or reactions to irritations are accompanied by, and doubtless related to, changes in the ionic calcium of the blood.

CHAPTER XXIX.

ETIOLOGICAL FACTORS IN DENTAL CARIES.

PROBLEM: What are the dominant etiological factors in dental caries?

INTRODUCTION AND DISCUSSION

We have seen from the foregoing chapters, the following very outstanding data regarding the conditions associated with the presence and absence of dental caries: First, individuals with a marked susceptibility to dental caries have at that time an increased susceptibility to rheumatic group affections, and this group tends in this condition to have a depressed ionic calcium of the blood; second, individuals without susceptibility to dental caries and with a susceptibility to periodontoclasia (pyorrhea alveolaris) tend not to be susceptible in this condition to rheumatic group lesions and tend to have an ionic calcium of the blood, normal or above; third, this latter group does not tend to have dental caries.

It seems, therefore, very probable that susceptibility to dental caries is linked very closely and directly with the calcium factor of the blood and saliva. To determine this, we have made a large number of both total and ionic calcium determinations of saliva and blood of individuals with and without dental caries. A careful clinical examination of these individuals reveals that the saliva in the mouths of the patients with the periodontoclasia (pyorrhea alveolaris) tends to be markedly on the alkaline side of neutrality, with an increase in alkalinity in the periodontoclasia pockets. It is a conspicuous fact that dental caries never occurs in periodontoclasia pockets at the time of the active process.

(Active absorption processes may resemble caries but they constitute a different phenomenon.) It is a most remarkable fact that, in general, the efforts that have been made to produce artificial caries have either been only partially successful or entirely negative. It seems apparent that some very fundamental elements in the process have not been provided for.

With this in mind I have chosen to attack this problem from a new angle. Since all proteins and colloids are now shown to act probably, stoichiometrically—that is, by the purely chemical force of primary valency—we may assume that with a change of the hydrogen-ion concentration from the alkaline to the acid side of the iso-electric point of that medium, we will have a change in the ion of that medium with which that substance will enter into chemical combination. We are quite familiar with the illustrations of the charged ions from a silver electrode, which is positively charged, disbursing from that electrode with their positive charges under the law, that like potentials repel, and unlike potentials attract.

When a tooth is bathed in saliva with pH above the iso-electric point of that saliva, it can combine only with the anions, which are metals and bases; or, when of a pH below this iso-electric point, will combine only with acid ions. If, however, the entire tooth or the majority of its surface is bathed in saliva of a Ph above the iso-electric point and at some point on the tooth there is, because of mechanical conditions, a lower hydrogen-ion concentration sufficient to be on the acid side of the iso-electric point, immediately two distinct changes have been established. In this latter condition there is a reversed polarity with the result that the tooth surface will be positive, the liquid in this restricted acid zone negative, while the balance of the tooth will be negative to a zone which is positive: namely, the surrounding saliva. This establishes a closed circuit battery. As ions of calcium compound are dissolved by the acid, they are charged with the same sign as the tooth and therefore repelled from it; and with increasing concentration of that acidity there is an increasing repulsion of the calcium from the tooth, whereas the normal environment of the tooth should be alkaline and the tooth and the calcium should be of opposite charge, and the tooth would therefore attract the calcium ions and that would, by the process of crystallization, build into and upon the tooth structure, if that alkalinity became sufficiently strong to make the potential charge greater than the

force required for the crystallization and ionization.

We have, then, the visualization of dental caries. The normal saliva is slightly on the alkaline side of the iso-electric point of saliva. The normal tendency is for calcium ions to have an opposite charge to that of the tooth structure and therefore will be attracted to it and the process of intensive calcification will go on by purely stoichiometrical processes, which must be recognized as slightly different from the metabolism, as we think of it, in cell function since there are no living cells present in this process.

Starches lodge in interstices of the teeth in which they are protected from the alkaline saliva in which, if not protected, they could not develop. Nor could the acid medium they generate remain acid if the normal saliva had free access to it to neutralize it. But proteins, such as the saliva, are amphoteric—that is, have the capacity of being either acid or alkaline—and this same saliva may be chemically very similar, except in relation to the compounds which will be built up and torn down by it, and from it. The lactic acid producing organisms, of which there are many, can in this environment produce a pH as low as 4 or even 3. This would make a marked difference of potential and completely reverse the forces between the tooth and the medium surrounding it. The organisms are, however, directly protected from the surrounding medium by an organized membrane, the bacterial plaque, which is a leathery substance, a result of chemical combination between an excretion of the organisms and the proteins of the saliva. As fast as these acid ions come through this membrane, they combine with the proteins of the saliva, producing substances which are insoluble in the saliva. The following factors are necessary for the maintaining of this condition. The alkali reserve of the saliva must be decreased, in general, to a point sufficient to make it possible for a still further lowering to be established and maintained at a point of bacterial protection of an acid producing bacterium of sufficient activity to change the local acidity of the saliva at the point in question well below the iso-electric point of that saliva. The organisms which do this must have a supply of starch or carbohydrate from which they produce the lactic acid for still further reducing the hydrogen-ion concentration.

In a normal condition of the mouth the factor of safety is sufficiently on the alkaline side of the iso-electric point of saliva to maintain a constant potential between the ionic calcium of the

saliva and of the tooth to keep calcium continually entering the tooth structure. Under certain conditions, such as fever, pregnancy, etc., this normal environment of the mouth is changed. Since every substance, when placed in a liquid medium, tends to produce ions of its structure in that medium, there is always maintained a balance between the forces, expressed as valency between ions, and the forces of solution and crystallization. In pregnancy this normal balance is broken through a change of environmental fluids, blood, and saliva; calcium goes out of the tooth under this law of ionization. Slowly but definitely the teeth lose some of their substance as ionic calcium compounds. The factor of safety being reduced, it is much more easy for local zones of bacterial growth to create a condition just over the iso-electric border on the side of relative acidity, with the effect that in such teeth, and with such an environment of saliva, the decay takes place very much more rapidly than in an ordinary mouth where the normal factor of safety is in general maintained. We must remember that acidity and alkalinity are relative factors dependent upon the iso-electric point of that individual's saliva. In case, then, the individual has a high ionic calcium of the blood, he has a high capacity for maintaining the alkalinity of the saliva; and this type of individual tends, as we have shown, to tear down alveolar bone about the tooth to maintain an extreme alkalinity, but in so doing produces an environment which accomplishes two things. It prevents dental caries by its large alkaline factor of safety and it tends to make the enamel of the tooth more dense than normal. This type of individual tends to have the glassy dentin on all surfaces of abrasion.

Our studies have shown, as have also the studies of others, that practically all teeth before eruption are in a condition in which the enamel will stain very perceptibly with silver nitrate and other stains, for an appreciable distance into the enamel, and that after eruption the enamel surfaces of the tooth undergo a change in which there is apparent increase in the density of the surface enamel so that they stain much less readily, and in old age and in all adult life free from caries, the surface layer of enamel is but slightly penetrable by silver nitrate. This process of hypercalcification (as I have chosen to term it) is pretty largely completed by the twentieth year of life, after which, except in periods of disturbed saliva, there is little tendency to dental caries.

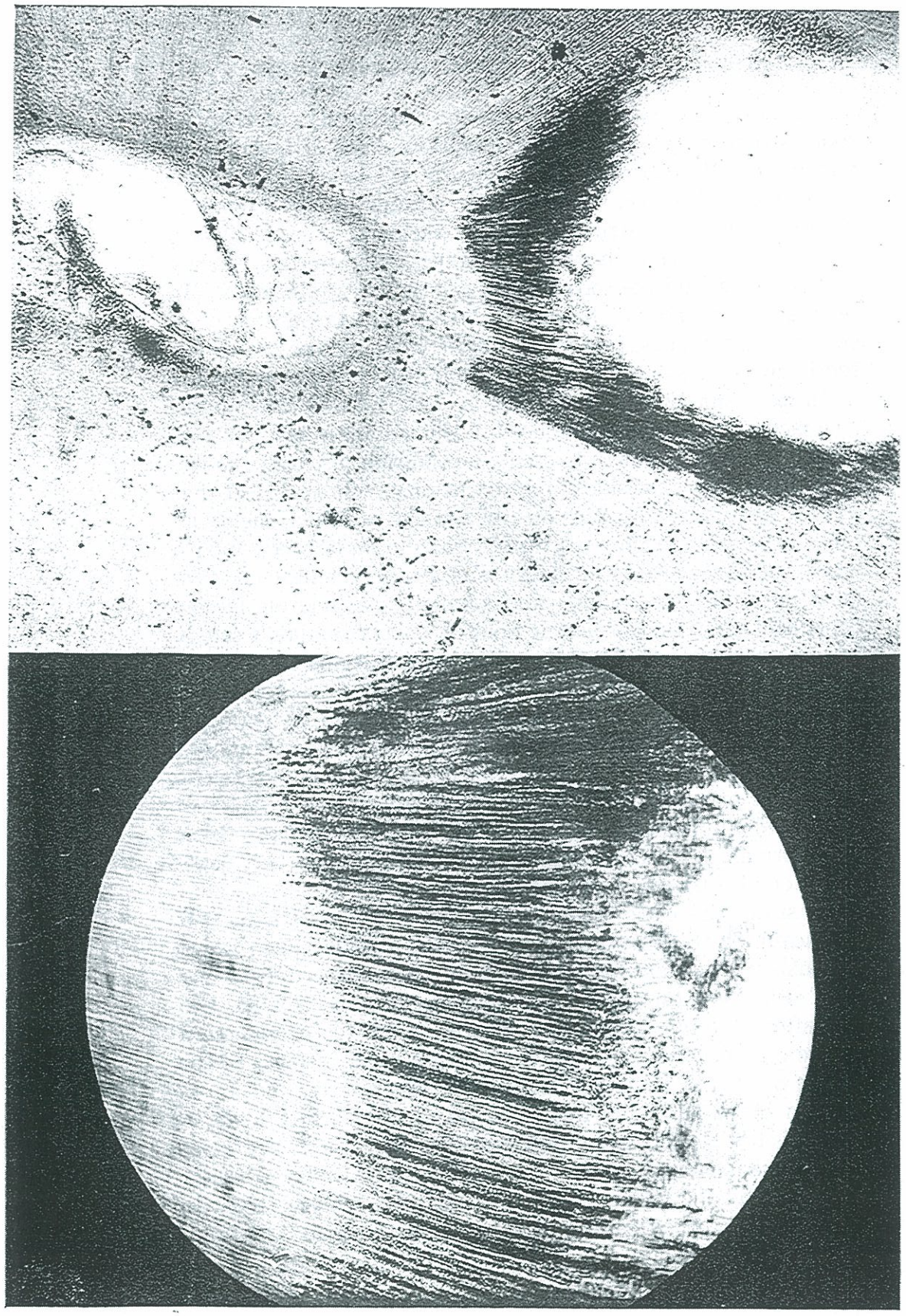


FIGURE 163. THE MICROSCOPIC APPEARANCE OF A SECTION OF A TOOTH WITH AN ARRESTED CARIES. TWO MAGNIFICATIONS.

We have, therefore, in the change of environment, as provided by the change in the hydrogen-ion concentration of the saliva, its iso-electric point, and its ionic calcium, factors which enter largely into the condition of immunity and susceptibility to dental caries. It is a quite frequently seen phenomenon that a mouth, in which caries has been active, has suddenly, ceased to be so, and *vice versa*. Among the factors which enter into life to bring about these changing states, are febrile disturbances, physical and nervous overload, and pregnancy. An illustration of the effect of the latter upon a tooth, is shown in Figure 163, which shows a cross section of the tooth with a deep caries extending nearly to the pulp. It will be noted that a secondary dentin has been thrown down on the pulpal surface beneath the approaching caries; and this caries, which at one time was active and progressive, ceased to be so, and there is a strong demarcation in cross section between the zone of living dentin and the dead dentin of the caries. The period at which this happened, as determined by the patient's report of the condition of the tooth, corresponded with the period of pregnancy and lactation, and this was an individual with normally a high defense. In the higher magnification shown, the etching out of the dentinal tubuli is very clearly disclosed; and it is both interesting and significant that, in this case, the zone of limitation of the advancement of the bacteria into the dentinal tubuli is distinctly marked. The irritation of the toxic bacterial products undoubtedly sufficed to produce the reaction within the pulp, which caused the laying down of the secondary dentin.

SUMMARY AND CONCLUSIONS.

Dental caries is dependent upon the following factors:

(a) A reduction in the hydrogen-ion concentration of the normal environment of the tooth.

(b) An acid producing bacterium.

(c) A change in the chemical constituents of the pabulum bathing the tooth.

CHAPTER XXX.

THE NATURE OF SENSITIZATION REACTIONS.

PROBLEM: Do dental infections produce sensitizations of an anaphylactic character?

EXPERIMENTAL AND DISCUSSION.

For several years, I have been seeing illustrations of systemic diseases, the chief characteristics of which were quite unlike those of ordinary bacterial invasion, and which seemed very definitely to be related to dental conditions. The following is the history of such a case previously reported by me.

The patient, a man about forty, presented with the following history. For two years he had been affected with recurring headaches followed by digestive tract disturbance (not preceded by it) and accompanied by lassitude; which made it practically impossible for him to carry on his business. For the last six months prior to his coming, he had been practically compelled to abandon his business, and was in a state of mental discouragement and depression as a result of his physical disability. An examination of his mouth showed very extensive periodontoclasia, and, bacteriologically, very profuse fusiform and spirochete infection. At our first sitting we curetted one-fourth of the mouth. Within a few hours he suffered a violent attack of his characteristic headaches, followed before morning by acute digestive tract disturbances, with purging, cramping, and mucous stools. This attack lasted for a couple of days. After it subsided, he reported that he felt better than he had for some time, and was convinced that the reaction was related to his dental condition and its treatment. In about five days the other half of the upper arch was curetted, which operation was followed by a similar reaction though less severe. Similarly, at intervals of about five days, the lower arch was curetted, one-half at a time, during which time he was continually improving. Soon after the gingival infection was obliterated, a couple of teeth, being considered too far advanced for treatment, were extracted. His health returned to normal and has remained so for ten years, except that on many occasions he has felt the beginning of the old symptoms returning, has pre-

sented promptly for treatment, and generally in proportion to his development toward the condition of sensitization, he responded in the same manner to treatment, though with much less severe reaction. He became so familiar with his symptoms that on several occasions he telephoned during the day saying, "I feel one of my old attacks coming on. How quickly may I have a treatment?" which would always be given at the earliest possible moment, sometimes within an hour or two. The treatment was successful in aborting the attack in proportion to the earliness in the attack when the treatment was instituted. Many forms of treatment were tested, such as the injections of emetin and succinimid of mercury, subcutaneously, which had but slight effect. We will refer to the nature of these symptoms in later paragraphs.

Another case with a similar sensitization complained because we did not do more of the curettage in gingival treatment at the first sitting; and when we advised her that she probably would have a reaction and to let us know regarding it by telephone the next day, she assured us that she would either telephone or come in. On the next day, she found herself feeling so miserable that she not only did not come to the office but did not even get up from her bed, even though the telephone was on a stand near the head of her bed. She said, "Well, what's the use of telephoning? He knew I would be sick anyway." She really did not have energy enough to reach the telephone, and report. Similarly, after her first acute reaction was over, she felt distinctly better. We have also reported previously, in the paper referred to, the cyclic nature of these sensitizations, some having a period of five or six weeks in the early stages, or even several months, with the periodicity shortening to two or three weeks, and finally even less.

Occasionally, though not generally, we found that after the extraction of infected teeth without gingival infections, the patients had very marked reactions which were more like toxic processes than bacterial invasions. A careful study of a large number of these cases suggested that this toxic factor was in many instances very important, and seemingly more important than the bacterial invasion factor. We, accordingly, instituted a long series of experiments to determine the nature and qualities of the toxic substances in teeth, if such existed, and their effects on animals both directly and in connection with the bacterial strain

SENSITIZATION REACTIONS TO TOOTH TOXINS

Group	No. in Group	Days Lived	Loss		
			Actual	%	% per day
Organisms washed and suspended in NaCl	8	7	203	18	2.6
Whole Culture Group I	16	6	209	18	3.0
Whole Culture Group II	55	7	226	20	2.9
Filtered Tooth Washings	13	5	191	19	3.8
Unfiltered Tooth Washings	8	12	221	22	1.8
Sensitized Rabbits	4	4	94	10	2.5

FIGURE 164.

found in these teeth. Figure 164 shows the results of these studies. It will be noted that in the group of animals inoculated with the washed organisms suspended in sodium chloride, the loss in weight per day was 2.6; and in the unwashed or whole culture, 3.0, the dosage being adjusted to approximately the same number of organisms: namely, the amount that would be in 1 cc. of a 24 hour culture broth. A second and larger group of 55 rabbits receiving the whole culture, had a loss of 2.9. The average length of time, however, that the animals lived in these three groups was approximately the same: namely, 7 in the first, 6 in the second, and 7 in the third. When, however, animals were inoculated with filtered tooth washings, the average length of life was 5 days for 13 rabbits, with a loss per day of 3.8 per cent; and with the unfiltered washings, they died on an average of 12 days, with an average loss per day of 1.8 per cent. In another chapter I have discussed the probable reason for the greater toxicity of the filtered washing than the unfiltered, as judged from the length of time the animals lived. When, now, we compare with these figures the effect of injection of the whole culture into rabbits that had been previously sensitized by injecting, intravenously, a small quantity of the filtered washings, (not the total quanity, as above, from the tooth in question and from the chips of which the organisms were grown for this whole culture), this remarkable result came out, that the average length of life of 4 rabbits so treated, was 4 days after the injection of this culture (Note that this is less than the average length of life of rabbits in any of the preceding groups) and the percentage loss per day, per rabbit, was 2.5. Two possible factors, at least, were possibly contributing, one a sensitization and the other an additive injury. The fact,

however, that some rabbits not included in this group, died within a few minutes or hours after being injected with the culture where they had previously been sensitized by the use of the toxic substance from that tooth, precludes, in those cases, the possibility of the explanation's being due to an additive factor, since they died from typical sensitization phenomena, such as scratching the nose, violent peristalsis of the intestines, labored breathing, etc. Another argument against this being an additive factor is the fact, that when succeeding injections below the lethal dose of a given culture are used in the same animal, it tends to build up defense, which, with most cultures, can be brought to a state of very high toleration, permitting of massive doses without lethal effects.

In the preceding chapters, 17 and 20, I have discussed the capacity of teeth for containing toxic and bacterial products, and have demonstrated that the quantity therein may be ample to produce very profound disturbances, both in animals and in humans. I have brought out the fact that approximately five per cent of even a well root-filled tooth is fluid, which may be culture media or toxic product; and also that when animals were inoculated with the bacteria-free soluble toxin derived from the infected tooth, they developed very definite and characteristic symptoms, and also that, in some instances, they were much more sensitive and susceptible to the organisms cultured from that tooth; that the toxic substance taken from teeth tended to disturb metabolism and start a procession of changes which usually terminated in death, and usually with marked changes in the digestive tract, with great loss of weight. In another chapter, we will study the structural changes of tissues as a result of these processes. It is, however, important to note here that, in some instances, an acute diarrhea was produced in from thirty minutes to two hours after the injection of this toxic substance, and animals not infrequently died having had blood-streaked mucous stools. It is, therefore, apparent that we are dealing with substances of profound toxicity. There are, however, many types of sensitization which differ from these expressions of toxicity. In one case, we are dealing with systemic poisoning from a violently acting toxin; in the other, with a state of exalted irritability of tissue, a true anaphylaxis or allergy. While this is not intended to be a treatise on immunology, it seems necessary for me to give a brief review of the conditions which obtain in true anaphylaxis.

When proteins are injected parenterally into suitable animals,

they may pass through the blood stream without any apparent effect. If, however, at a subsequent date, particularly from six to twenty-eight days after this first injection of protein, which may have been a very small dose, there is again injected into the circulation of that animal some of the same protein, it will produce an entirely different effect. In many instances there will be disturbed breathing, itching of the skin, itching of the nose, and if the animal is particularly sensitive it may die in a few minutes from spasms of the bronchioles, with continuation of cardiac function after the cessation of respiration, or the animal may entirely recover. The processes that have developed are somewhat as follows:

The first or sensitizing dose sets up in that animal the development of an active mechanism capable of splitting that protein, in order that it may be eliminated from the blood. The first or sensitizing dose may have floated in the blood stream largely for days before that mechanism had been sufficiently perfected to split it. With the consummation of that mechanism the animal was able to split large quantities of this protein in a short time; but since, according to Vaughn, all proteins split into a poisonous and non-poisonous part, the poisonous part being the same in all proteins, there is set free in the system a quantity of poison which, if not immediately eliminated, does harm by its presence. This constitutes the sense of illness from disease and the cause of pyrexia. Vaughn states that the amount of poison in a gram of cheese, when thus split, is sufficient to kill seven hundred guinea-pigs. The first or sensitizing dose may in some instances be only a minute fraction of a gram and yet be sufficient to prepare the body to react vigorously against a second dose. The introduced protein is spoken of as the antigen and the substance which the body develops as the antibody. An illustration of the extreme delicacy of this mechanism is familiar to all in hay fever. The individual who suffers from hay fever is usually sensitized to the pollen of some weed, grain, or flower, and the amount that is necessary to bring on a reaction is so infinitely small, that it may drift invisibly in the air and doubtless can be less than a millionth part of a gram. In Part Two, under Other Tissues, we give illustrations of anaphylaxis to dental infections in addition to those given here.

With these fundamentals of protein sensitization in mind, let us review the following case from practice: The patient presents with a history as follows: For some time he had been suffering

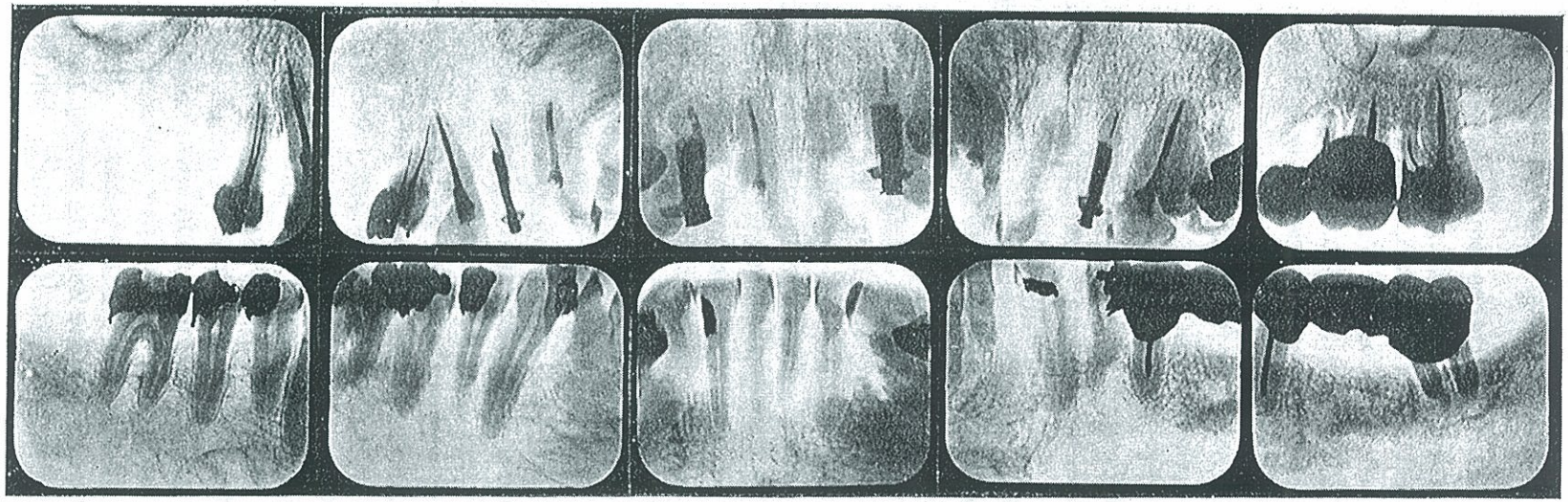


FIGURE 165. ROENTGENOGRAPHIC APPEARANCE OF THE TEETH. PATIENT SUFFERING SENSITIZATION REACTION FROM HIS DENTAL INFECTION, SHOWN IN FIGURE 166.

from recurring attacks which were increasing in severity and frequency, closely resembling hay fever but not related to any season or locality. Careful and exhaustive studies had been made by specialists in different cities to find the nature and cause of his sensitization, without avail. Figure 165 shows roentgenograms of his teeth which have evidently been infected for years, but have given him very little inconvenience or disturbance. Upon the extraction of the first tooth, he developed, within six hours, the most severe attack of his sensitization reaction he had ever had. Figure 166 shows his appearance which lasted for days. His eyes were bloodshot; tears would drip from his eyes; and the mucous would almost stream from his nostrils. His headache was extreme. The inflammation involved all mucous membranes of the mouth, nose, eyes, and throat, and extended around his eyes, nose, and mouth, approximately half an inch. The night of his first attack he did not sleep a moment, according to his report, and his distress was pathetic. The use of mild sprays, carrying adrenalin and cocain, greatly relieved his suffering. The tooth that was extracted was cultured, and the toxin washed from it injected into two rabbits. Both developed extreme inflammations. In one the eyes were bloodshot and tears running in forty minutes; and for two days profuse discharge was coming from its nostrils, shown in Figure 166. Note: This animal is not reacting from anaphylaxis, not having been previously sensitized. It is apparent that we are dealing here with a substance which has profound tissue affinity, and which is not bacterial, though it may be a bacterial product, since the fluid injected into the rabbits had been passed through a Berkefeld filter and was bacteria-free. Subsequently, the balance of the infected teeth were removed, a few at a time, without serious reaction, and the patient's health very rapidly and splendidly improved, and for a year he has been without a single recurrence of his old and troublesome affection. Since the reaction in the rabbits was produced by the filtered washings of the tooth, we cannot interpret their disturbances as a tissue affinity quality of a particular bacterium injected.

A striking illustration of an anaphylactic state or sensitization produced in a rabbit is as follows: Rabbit 184 was inoculated on Feburuary 18th with a salt solution washing of two crushed teeth, (biscuspids,) intravenously. Its weight at this time was 855 grams. On the 23rd its weight had increased to 920 grams, and on March 1st to 1046 grams. On March 2 it was inoculated

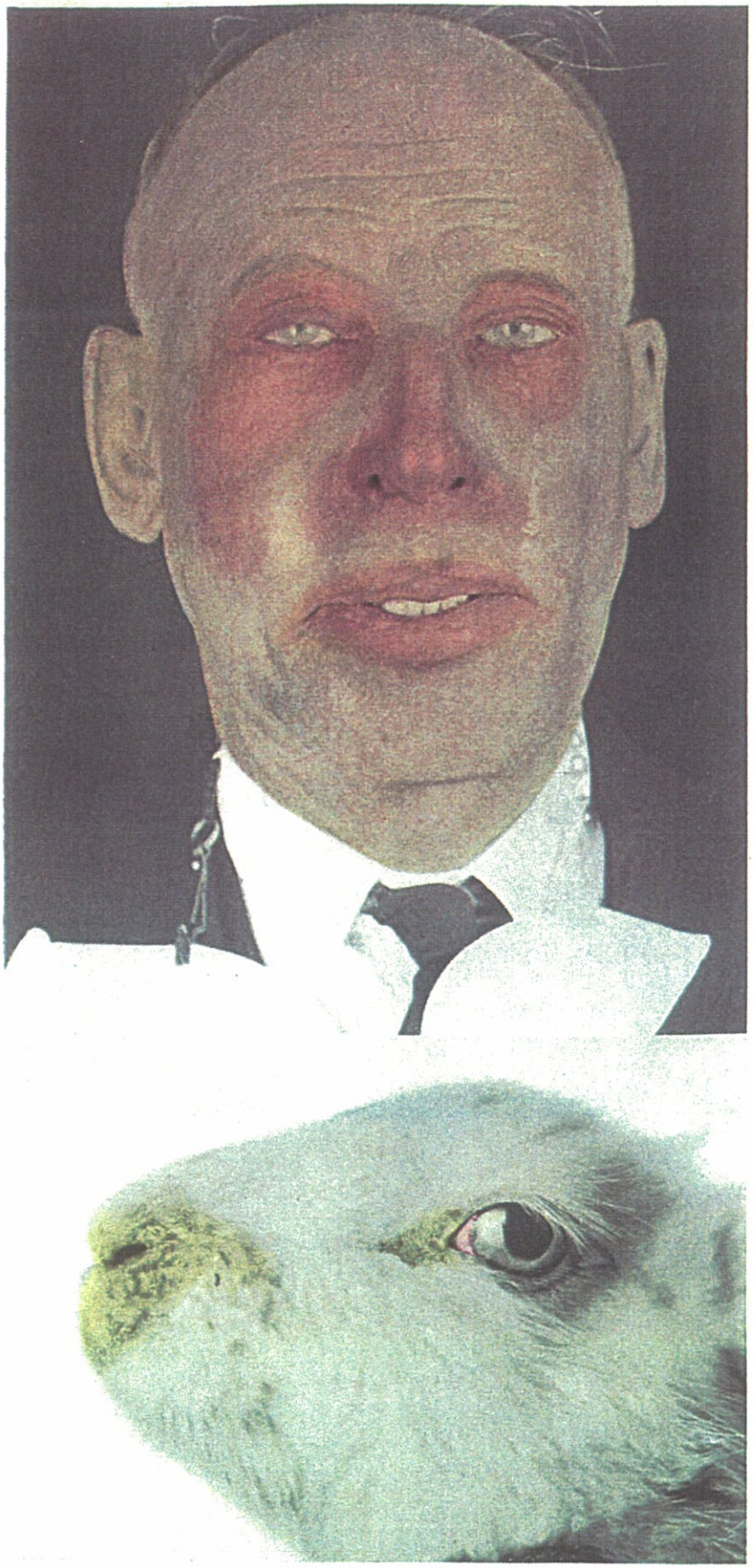


FIGURE 166. A, A RECURRING ACUTE INFLAMMATORY SENSITIZATION REACTION PRODUCED IN A PATIENT BY HIS DENTAL INFECTION; B, A RABBIT WHICH DEVELOPED ACUTE LACRIMATION AND RHINITIS IN FORTY MINUTES AFTER INOCULATION WITH WASHINGS FROM THIS PATIENT'S CRUSHED TEETH.

with the culture grown from these same teeth; weight 1075 grams. Within three hours after the inoculation of approximately 1 cc. of the whole culture, which is the bacterial suspension in the media in which they were grown, the rabbit died. The postmortem examination showed the liver to be slightly enlarged, stomach normal but very pale in color, lymph glands surrounding the stomach markedly enlarged, edematous, and resembling grapes, spleen enlarged, and lungs collapsed. The diagnosis of cause of death was anaphylaxis.

The literature and teaching of the past have placed a particular emphasis on certain groups of symptoms as being characteristic of sensitization, expressing themselves chiefly in the skin, air passages, and bronchioles. We have, accordingly, been in the habit of looking for symptoms as the chief ones expressive of anaphylactic reactions. We are, however, coming to believe that many tissues respond with true anaphylactic reaction which we have not regarded as likely seats of this allergy.

Inasmuch as individuals sensitized to foreign proteins have certain definite reactions to that foreign protein, we have made animal studies to determine whether the introduction of the toxic substances taken from the teeth would develop in animals a state of anaphylaxis which could be demonstrated by dermal and other reactions. We have found that the toxic substance taken from some teeth, when injected into rabbits, does produce in from six to twenty-eight days a true state of anaphylaxis, as evidenced by the fact that they showed definite dermal reaction to either the placing of the toxin on a scarification or the injection of a minute quantity of it in the superficial layers of the skin. We have found also that in some cases this toxic substance sensitizes the animal not only to this toxic substance which, though bacteria-free when injected, prepares that animal to respond to a washed suspension of the organisms grown from the tooth which produced that toxin, but also to the culture medium in which those organisms have grown. A rabbit inoculated with a bacterial suspension grown from the tooth from which the toxin was extracted to sensitize that rabbit, when the suspension was inoculated into this rabbit, died within two minutes showing the classical symptoms of shock, or true anaphylaxis. Studies of this problem on several hundred rabbits reveal that all infected teeth do not have this toxic substance in the same quantity nor do they have the same qualities. Those familiar with the problem of sensitization reactions in

animals understand that the rabbit is not a favorable animal to use for this investigation, in that it is not highly sensitive to anaphylactic reactions as compared with the guinea-pig. We have used both guinea-pigs and rabbits. Particularly because of our other observations with which we wanted to make comparisons, such as elective localization of the organisms involved, we decided to use the same type of animals for our sensitization tests. We have deemed that there would be some advantage in not using animals that are too sensitive to anaphylactic reaction.

The recent literature has stressed the relationships between anaphylaxis and shock, and these in turn with reaction effects of animals inoculated with histamine. With this latter the animal dies from failure of respiration, usually in a few minutes after injection, during which time it exhibits a group of symptoms very similar to those exhibited by animals dying from anaphylaxis from the injection of a protein to which they have been previously sensitized. All such animals exhibit characteristic disturbances of the lungs and viscera, as marked engorgement of the capillaries and mesentery and visceral arterioles.

Figure 167 shows the normal vascularization of the mesenteries and intestines of a rabbit. Note the blanched white condition of the mesentery and the constricted blood vessels of the intestine. The specimens shown in Figure 168 are from a rabbit dying from a sensitization produced by crushing the tooth, injecting this into a rabbit, and later the rabbit was inoculated with the culture grown from this same tooth. This rabbit died in two minutes with the characteristic reactions exhibited in anaphylaxis. In the inoculation of over fifteen hundred rabbits for various purposes, no rabbits have died quickly, following inoculation as this rabbit has done, except where previously sensitized by such a process as this inoculation with the washings of a crushed tooth. Note the engorgement of the blood vessels of the intestines and mesenteries. Figure 169 shows the same condition in the similar tissues of a rabbit inoculated with histamine.

This condition is not comparable to the reaction produced in the rabbit injected with the material taken from the tooth of the patient referred to above shown in Figure 166, which symptoms developed about forty minutes after the first injection, since that rabbit was not sensitized by a previous injection. This reaction was probably a tissue irritation and in addition an elective localization. In other words, the rabbit shown in Figure 166 is not an illustration of allergy or anaphylaxis.

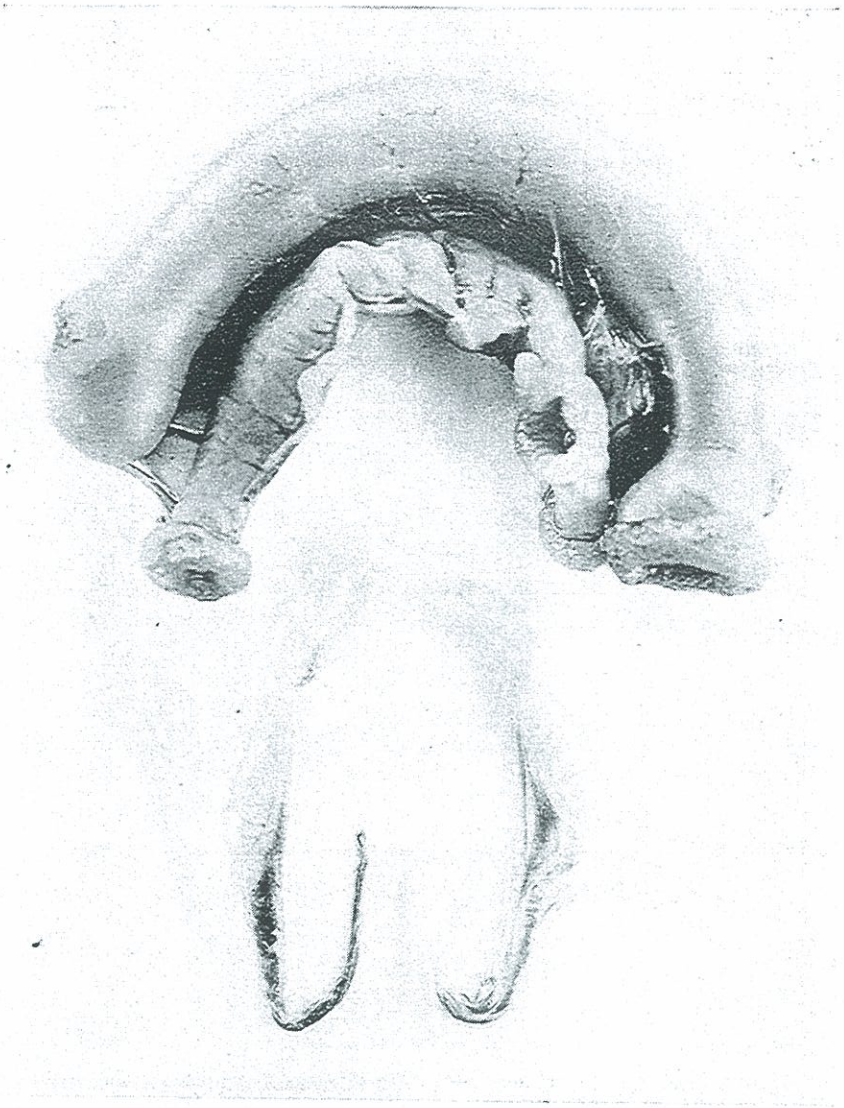


FIGURE 167. NORMAL VASCULARIZATION OF MESENTERIES, INTESTINES, AND TESTICLES OF A RABBIT.

In studying the skin reactions of animals, we have found two distinct types: First, appearing in from a half minute to thirty minutes and subsiding in a few hours, characterized by a central wheal from a fourth of an inch to one inch in diameter, which is raised, edematous, and hard, and surrounded by an erythematous area from a half inch to an inch and a half in diameter, as shown in Figure 170. We have also found a secondary reaction developing in from six to eighteen hours, which may last for a few hours or

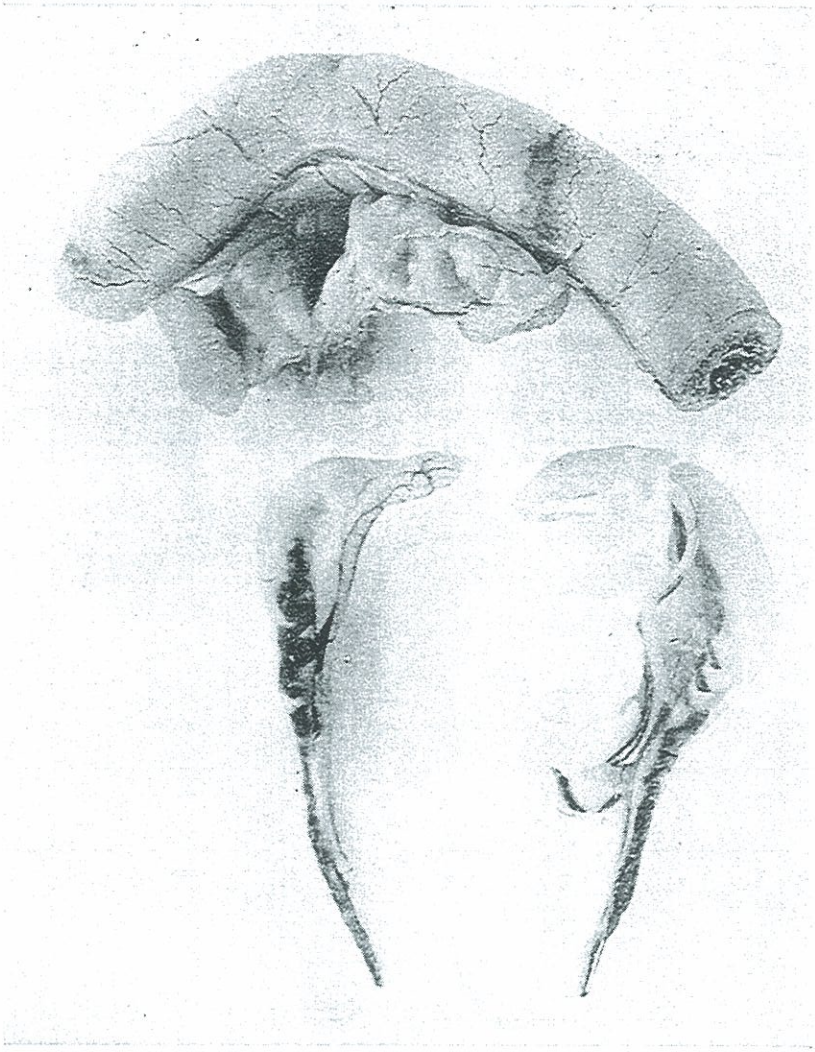


FIGURE 168. THE VASCULARIZATION OF MESENTERIES, INTESTINES, AND TESTICLES OF A RABBIT SENSITIZED WITH THE WASHINGS OF A CRUSHED TOOTH.

for several days, and in which the area originally occupied as the central whitish wheal is now deep pink and surrounded by a more or less deep pink area, often with an increase of temperature of the surface and the appearance of a scald or burn that is just short of the production of the water-blister. These vary in intensity. These are the characteristic reactions that make up the Schick test for the identification of diphtheria, as expressed in the first reaction, and the tuberculin test for tuberculosis as expressed in the second reaction.

Having demonstrated the presence of this condition and reaction in animals, we have made tests upon many patients to

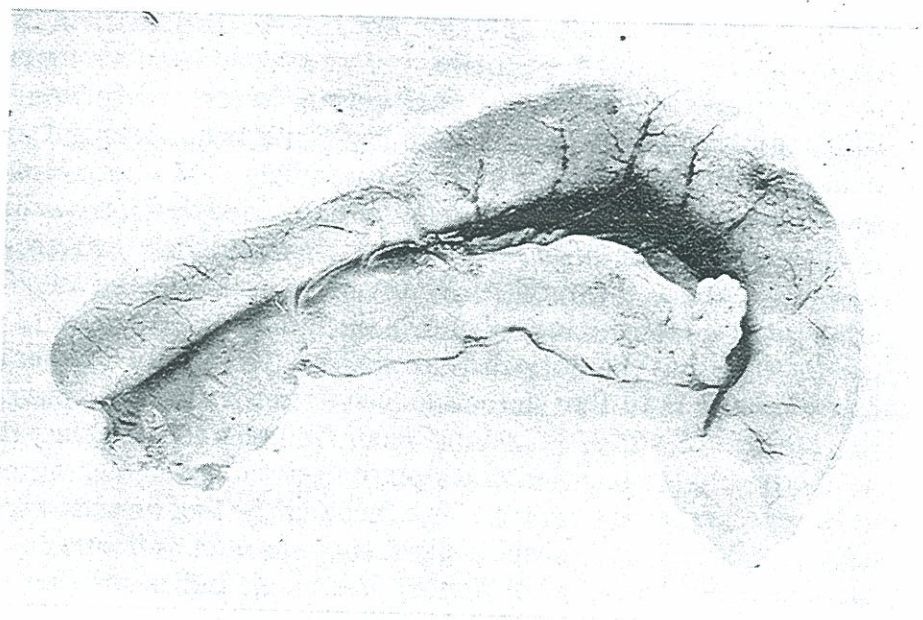


FIGURE 169. THE VASCULARIZATION OF THE MESENTERIES AND INTESTINES OF A RABBIT INJECTED WITH HISTAMINE.

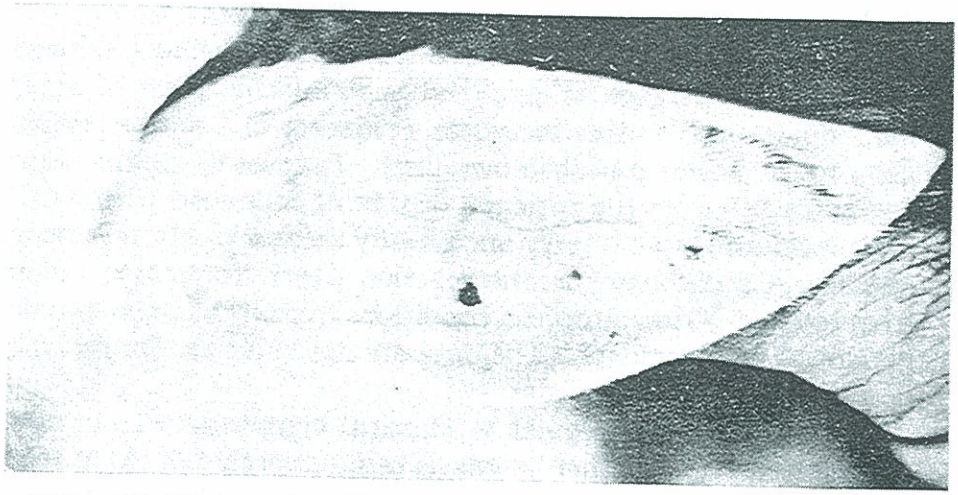


FIGURE 170. TWO MILD AND ONE STRONG POSITIVE REACTIONS IN A RABBIT'S EAR THAT HAD BEEN SENSITIZED TO A DENTAL TOXIN.

determine whether or not they would develop either or both of these reactions. Figure 171 shows the primary reactions of the patient shown in Figure 166, when tested with the extract of the toxin from his tooth, prepared by three different methods. Figure 171-B shows this same arm with its secondary reactions. The essential

features about this patient's case are that he had recurring attacks, cyclic in nature, the periods of which had been shortening for years and which latterly had become weekly or biweekly. This readily eliminated the possibility of its being seasonal and related to pollens, etc. If it be a true allergy, the dermal test should give the typical Schick reaction, provided that it is possible to extract the toxic substance which is producing the antigen, or which is acting as the antigen. Many methods have been used for extracting the sensitizing substance, including those generally in use for selecting the antigen from pollens, foods, etc. We have here evidence both that the patient is suffering from a true allergy, the antigen of which is coming from his infected teeth; and the antibody-antigen reaction takes place in the mucous membranes of the eyes, nose, and mouth. The fact that he had no recurrence for a year afterward, except a slight suggestion of an irritation at the time of the hay fever of August, is a strong indication that his primary disturbance was of this origin. It will also be noted that this patient had a strong secondary reaction from this original test and which reaction none of the controls of the six members of the staff developed, an additional evidence that we are in this case dealing with a specific reaction to a specific antigen.

In many of these cases we have found the patients sensitized to the toxic substance as extracted from infected teeth of other individuals, and in other instances, evidences of a marked specificity to the infection of their own teeth. In cases where the toxin was extracted from the patient's own tooth, the test, when positive, developed more rapidly and usually more severely. We have also found a difference in the reaction effect from toxin taken from teeth of periodontoclasia conditions from those with chronic periapical involvements. The data are not sufficient for making deductions or generalizations.

In addition to the regular or classical symptoms we are now coming to recognize other lesions as being directly related as true allergies. Conspicuous among these are skin disturbances, expressing themselves as dermatoses which may be very persistent and painful. Such a one is shown in Case No. 1334, a professional pianist who became incapacitated by the presence on the palmar surfaces of his hands of a scaly dermatosis accompanied by marked stiffness of his fingers. His hands would crack to or near the point of bleeding. (See Figure 172-A before treatment; and,

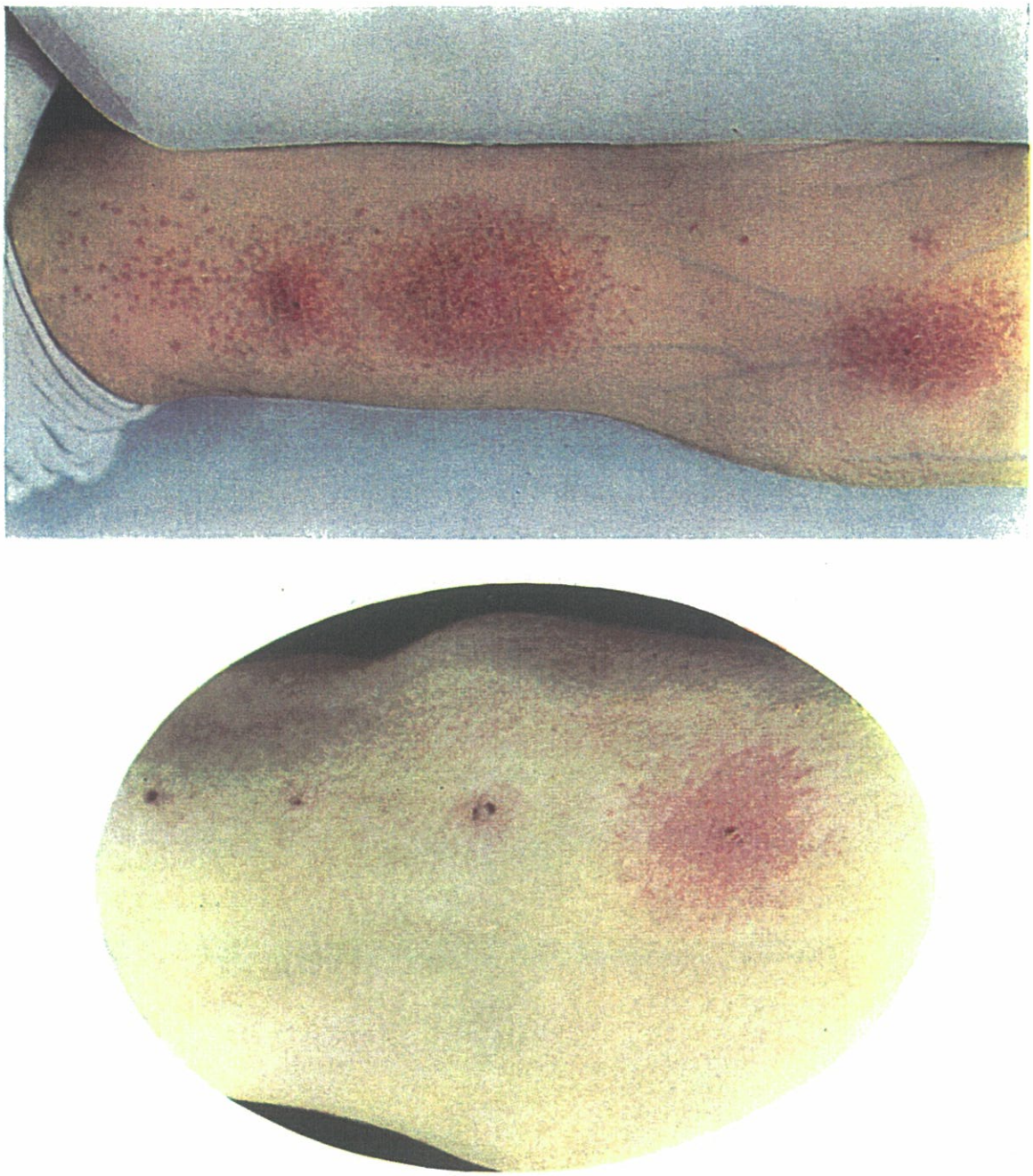


FIGURE 171. UPPER. THREE POSITIVE PRIMARY DERMAL REACTIONS ON THE ARM OF THE PATIENT SHOWN IN FIGURE 166. LOWER. ONE POSITIVE SECONDARY REACTION FROM SAME PATIENT.

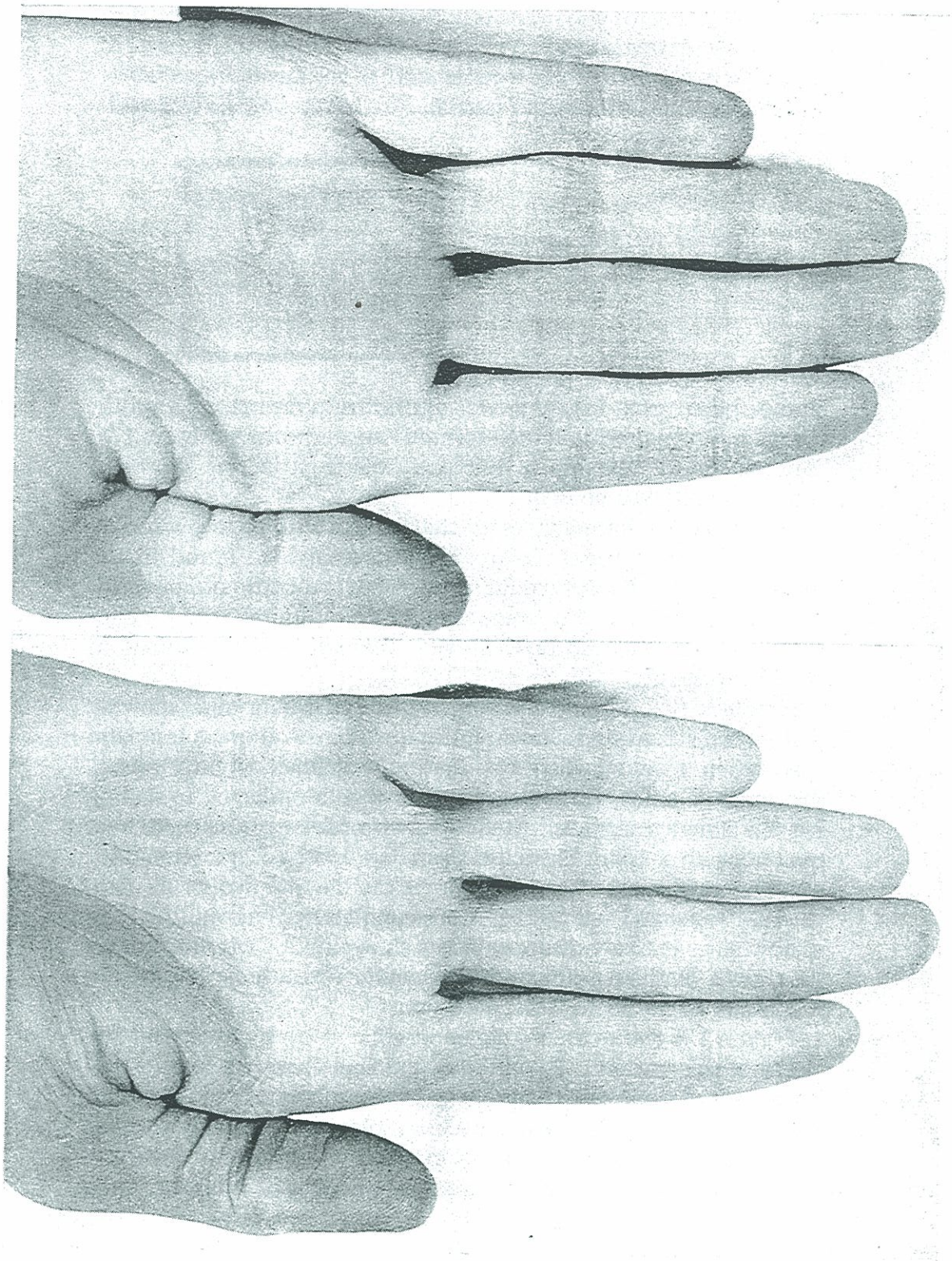


FIGURE 172. A SCALY DERMATOSIS, WITH MARKED STIFFNESS OF FINGERS. A, UPPER, BEFORE REMOVAL OF DENTAL INFECTION; B, LOWER, AFTER.

172-B, after treatment.) The condition did not respond to medication. The extraction of an infected tooth, shown in Figure 173, completely eliminated his trouble, and at the same time a condition of lassitude and mental languor. An extract of the toxic sub-

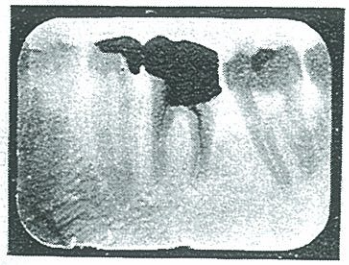


FIGURE 173. THE DENTAL INFECTION INVOLVED IN THE SKIN LESION OF FIGURE 172.

stance taken from his tooth was applied as a dermal test and in thirty minutes produced the enormous wheal shown in Figure 174. The secondary reaction in this case was negative, as shown in Figure B of the same figure.

These studies have suggested that the toxic substance which is present in the patient's body, might possibly be found in the patient's blood, if a test could be developed which would be sensitive enough to record it, since, apparently, infinitely small quantities are adequate to produce very marked tissue reactions in sensitized tissues.

Another type of skin reaction, typical of this group, showing dermal sensitization is shown in Figure 175. A shows a lesion on the patient's elbow which was distinctly defined, slightly raised, brownish in color, without erythema, with a tendency to scaling on the affected surface. B shows two positive primary dermal reactions to a toxin extracted from his tooth. The secondary reaction in this case was negative. After the removal of his dental infections and before they were completely removed, his skin disturbance entirely disappeared as shown in C. My interpretation both of these primary and secondary reactions is given in Chapters 45 to 56 on Interpretation.

Figure 176 shows the roentgenographic record of some of the teeth of this patient. It will be noted that there are very extensive areas of bone absorption, both at the gingival borders and at the root apices. The local dental pathology corresponds with his clinical history. He is a man of unusually high defense, and has carried this large amount of gingival and apical infection for a

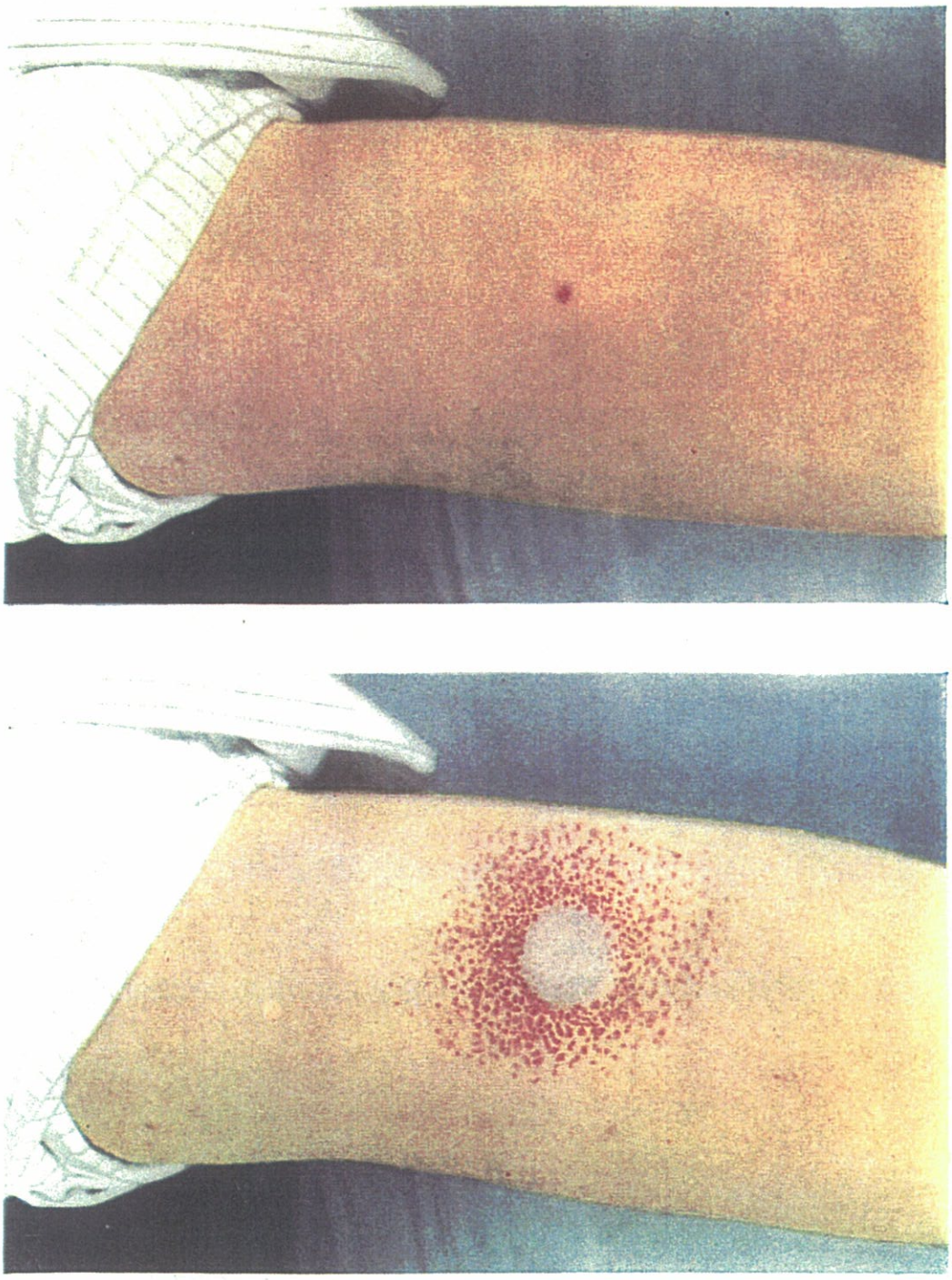


FIGURE 174. THE DERMAL REACTIONS OF THE PATIENT IN FIGURES 172 AND 173. LOWER, POSITIVE PRIMARY; UPPER, NEGATIVE SECONDARY.

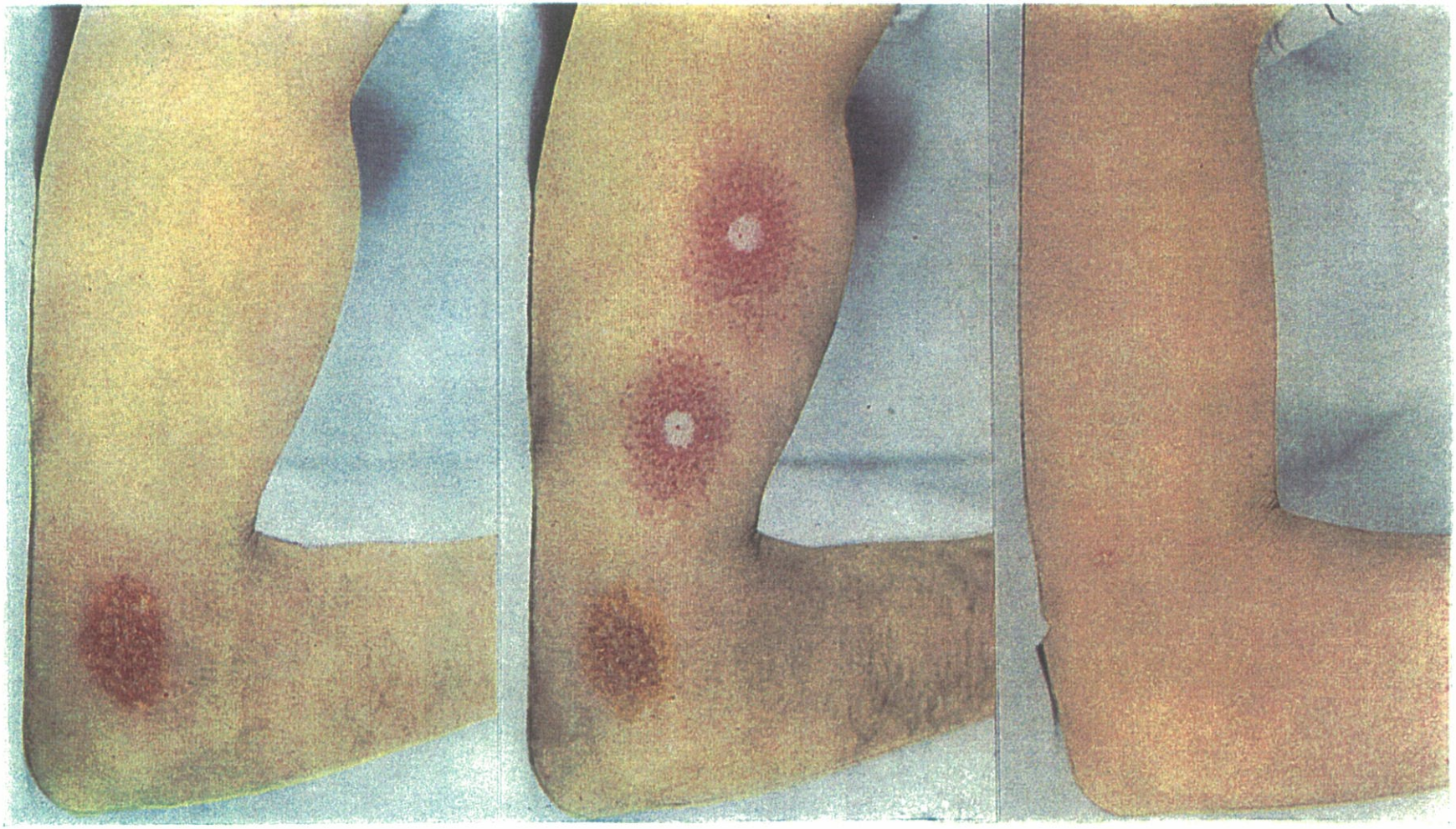


FIGURE 175. FIRST, A PERSISTENT DERMAL IRRITATION; SECOND, THE SAME ARM WITH TWO PRIMARY POSITIVE REACTIONS FROM HIS DENTAL INFECTION; THIRD, THE SAME ARM ONE WEEK LATER. THERE WAS NO RECURRENCE IN NINE MONTHS.

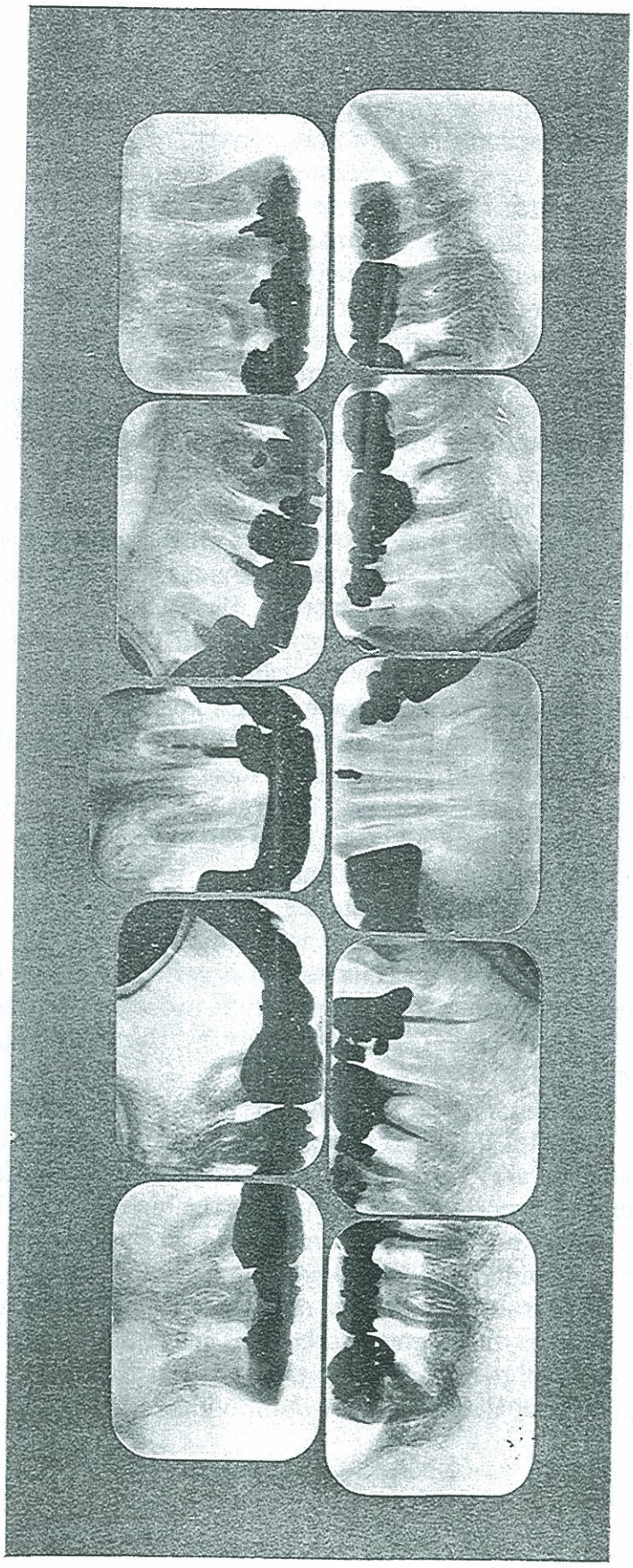


FIGURE 176. ROENTGENOGRAPHIC RECORD OF THE TEETH OF THE PATIENT SHOWN IN FIGURE 175.

number of years. A constant passage into his system of the irritant protein compounds from these teeth, seems to have created a state of hypersusceptibility and reactivity.

At this point I wish to discuss an important phase of the cases which, so far as we know, is entirely new. When we compare the type of systemic disturbance with the researches on the variations in chemical constituents of the blood, this important new fact has come out. In a group of individuals suffering from typical sensitization reactions, we found that the type of dental pathology, as expressed in the mouth, is that of extensive or marked rarefying osteitis, which I have interpreted as indicating an active reaction locally about the source of infection, and which active and vigorous reaction is a good sign and constitutes the quarantine station protecting the patient. But this extensive absorption of alveolar bone, as revealed in the roentgenograms, did not take place lately, but years previously; and in all probability, as indicated from the history, for a long period of time these individuals did not have anaphylactic reactions from these processes. In studying the ionic calcium of the blood it was noted that these individuals have a high normal, usually above normal, whereas the individuals suffering from the typical rheumatic group lesions generally had an ionic calcium of the blood, at the time they were suffering from their rheumatic group lesions, which was below normal, frequently considerably below.

I have found one type of rheumatism which appears to be present only in individuals having a pathologically high ionic calcium. Histopathologically, it is quite a different type of reaction from that of the arthritides. It is generally characterized by degenerative, rather than proliferative, processes, which sometimes are revealed roentgenographically by the radiolucency of the bones.

Since it is demonstrated that this quality of anaphylactic reaction to dental infection occurs only in individuals who have had a history of very high defense against streptococcal infections and rheumatic group lesions, we have in the histories of all of the patients, shown in this group, evidence of an overload of dental infection in an individual with a high capacity for reaction, which overload of dental infection was maintained for a long period of time. The effect has seemed to be that inasmuch as one of the first principles of defense is the capacity to reacting to a relatively small quantity of the irritant, these individuals developed so sen-

sitive a mechanism of reaction that when the local barrier began to break down immediately about the infected teeth, those tissues which were most easily capable of developing an exalted reactivity, disclosed the presence of this toxin which had laterally become able to pass into the system, and they have thereby suffered a more or less constant state of exalted reactivity in these very reactive dermal tissues. So far as I know this is the first time this evidence has been observed, suggesting a simple interpretation of the nature of the anaphylactic reaction in these individuals. I have discussed this further from this standpoint in the next chapter on Precancerous Skin Irritations.

In order to study the capacity of toxic substances extracted from infected teeth for sensitizing rabbits to extracts made from the cultures grown from the same teeth, I have inoculated animals with these products with results shown in the chart in Figure 177. Rabbits 789 and 790 were controls; and it will be noted that they did not show skin sensitizations to the extracts from any of these products; whereas, Rabbit 814 showed an anaphylactic reaction to a sodium hydrate extract from the culture grown from the teeth of another patient; and in Rabbits 846, 847, and 848, we find all three rabbits, which have previously been injected with the toxic extract taken from this individual's teeth, were all sensitized and gave anaphylactic reactions to the sodium chloride filtrate to the extract of the whole culture grown from the teeth of this same patient as shown in Rabbit 846; and Rabbit 847 showed a reaction to the sodium hydrate extract from the culture grown from the teeth of this patient, and in Rabbit 848 the same condition. Whereas the tests for the extracts made by all the other methods were negative, these latter two were positive in sixty minutes and lasted for two hours.

Another group of rabbits was tested by using as our extract the toxic substance obtained from some recently extracted infected teeth from several different patients. These showed different reactions to extracts made by different methods. Whereas Rabbit 778 reacted to the extract of the whole culture, Rabbit 780 reacted to the powder obtained from the dehydrated washings, Rabbit 781 to the whole culture and the powder obtained by dehydrating and washing, and Rabbit 779 to the powder and the whole culture.

DERMAL SENSITIZATIONS DEVELOPED IN RABBITS

A. Ear used as Test.

Rabbit No.	Weight	Date of Inoculation 1922	Material	Date of Test 1922	Weight	NaCl			NaOH			Time Factor			Pathological Findings
						Filtrate	Polyvalent	Culture of 1237	Filtrate	Polyvalent	Culture of 1237	15 min.	60 min.	2 hrs.	
846	1205	3–1	Filtered washing	3– 7	958	+	—	+	—	—	—	—	—	+	Abscess cecum. Muscle atrophy. Paralysis of muscles, small intestines?
847	1060	3–2	Filtered washing	3– 7	983	—	—	—	—	—	+	—	+	+	Emaciation. Muscle atrophy.
848	962	3–2	Filtered washing	3– 7	715	—	—	—	—	—	+	—	—	+	Emaciation. Muscle atrophy.
814	948	1–4	Washed culture	2– 9	905	—	—	—	—	—	+	—	—	+	Pneumonia. Abscesses kidney. Cysts ovaries.
789	791	1–20	Culture	1–26	849	—	—	—	—	—	—	—	—	—	No gross pathology found.
790 Control	1040	1–26	Filtrate from culture, intra-muscular	1–26		—	—	—	—	—	—	—	—	—	No gross pathology found.

B. Abdomen used as Test.

Rabbit No.	Weight	Date of Inoculation 1922	Culture No.	Date of Test 1922	Weight	Rt. Side Abdomen			Lf. Side Abdomen			Control	Time Factor				Pathological Findings
						Powdered organisms	Powdered washing	Whole culture	Powdered organisms	Powdered washing	Whole culture		10 min.	60 min.	2 hrs.	3 hrs.	
778	1035	1–10	{572 575	1–19	998	—	—	+	—	—	—	—	+				No gross pathology found.
780	1389	1–10	{572 574	1–19	1290	—	+	—	—	—	—	—	—	—	+	+	Purulent arthritis, knee joints.
781	854	1–10	{572 575	1–19	772	—	—	+	—	+	—	—	—	—	+	+	No gross pathology found. Coccidiosis.
779	1337	1–10	{572 574	1–19	1221	—	+	—	—	—	+	—	—	—	+	+	No gross pathology found.

FIGURE 177.

SUMMARY AND CONCLUSIONS.

In summarizing these studies of sensitization we desire to present the above data as a preliminary report, for much of the information is not ready for interpretation. Some important facts, however, should be noted. In the first case presented with acute inflammation of the nose, throat, lips, and eyes, the extract which was taken from the tooth and which produced such violent reactions in the patient in thirty seconds to two minutes, produced practically no reactions in any one of six members of the staff treated similarly at the same time, which clearly indicated that we were dealing with a specific reaction.

From these data we are led to conclude:

(1) That teeth contain substances other than bacteria to which the individual may become sensitized, and which substances may, in addition, have strong toxic properties.

(2) The evidence here presented suggests that dental infections are capable of producing in an individual a state of anaphylactic sensitization, which condition may entirely and apparently permanently disappear with the removal of the dental infections. These disturbances may occur in dermal tissues, mucous membranes of the nose and throat, lacrimal tissues, mucous membranes of the bronchioles and air passages, as asthma, and the mucous membranes of the digestive tract and a number of other types of tissues.

CHAPTER XXXI.

PRECANCEROUS SKIN IRRITATIONS.

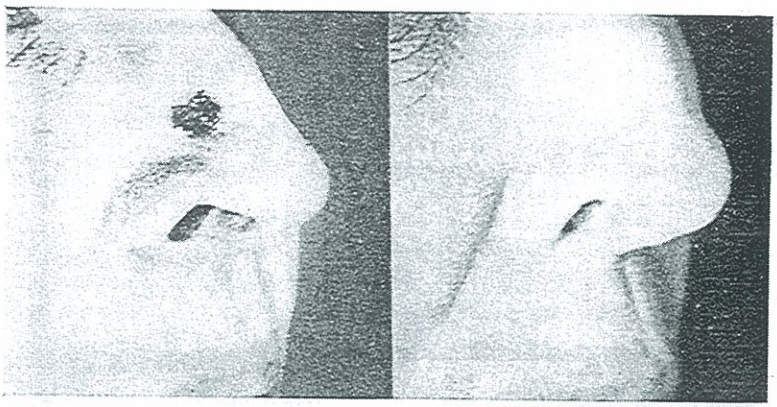
PROBLEM: Are there relationships between precancerous skin irritations and dental infections?

EXPERIMENTAL AND DISCUSSION.

In the preceding chapter the researches disclosed that dental infections may produce in individuals very marked anaphylactic reactions in various tissues of the body. It was also revealed that there is a relationship between the dental infection, the ionic calcium of blood, and the patient's history of a quite complete absence of rheumatic group lesions, and that this condition developed only in individuals having a normally high defense against streptococcal lesions. A frequent site of these lesions was shown to be the skin which is one of the first tissues to react to anaphylaxis. This has led us to a consideration of some of the types of skin lesions which have tended to recur and persist, and in time, occasionally, or in some types frequently, have taken on premalignant or definite malignant tissue types.

Before proceeding with this discussion, I want to forestall misapprehensions and misrepresentations which are very likely to be unintentionally made. I am endeavoring to be very careful not to say that dental infections have been shown to be the cause of cancer. I am trying to illustrate that since cancerous growths develop in chronically irritated tissues, the data I am here presenting suggest only that dental infections may, in this indirect way, be contributary to these states of irritation.

Figure 178 shows such a case. This patient had suffered for months from a lesion in the skin of her nose which had been diagnosed as a skin cancer. The roentgenograms of the teeth of this case are shown in Figure 179. It will immediately be noted that this individual had extensive areas of absorption for a long period of time (for thirty-four years as evidenced by the history) and at fifty-two years of age she is developing this persistent lesion on the side of her nose. It has tended to fluctuate, varying in severity but never entirely disappearing, usually carrying a thick angry looking scab. We prepared a note for her, directing her to



A B

FIGURE 178. SKIN CANCER OF THE NOSE AND ITS APPEARANCE THREE WEEKS LATER AFTER REMOVAL OF DENTAL INFECTIONS. SEE TEXT.

a cancer specialist for its treatment with radium. Almost immediately following the obliteration of her dental infections the red border surrounding it disappeared and it showed evidence of rapid healing. B is a photograph of the lesion three weeks after the making of the photograph shown in A. Her nose cleared up so completely that, as shown in the picture, it was difficult to detect where the original lesion had been. The lesion remained healed for five months when it showed slight tendency to return, at which time she was taken to the cancer specialist who gave it two treatments with radium, since which there has been no recurrence.

We shall not presume to interpret this history, but present the suggestion that if this patient was sensitized to her dental infection in such a manner as were the individuals shown in the preceding chapter, it is not impossible, nor even improbable, that the dental infection had direct relation, whether as a primary or as an additive factor, in the etiology of the lesion on her nose. If it may be that the state of abnormal cell proliferation is due to liberation of some toxic substance from the focus, set free in the system that has a high capacity for reaction to it, taking on a state of sensitization, it is not impossible that an additive factor may thereby be furnished, if not a primary causative factor, in the development of a neoplastic proliferation, in support of which suggestion I will present the following.

When these individuals are sensitized, for this individual was suggested to be from her dermal reaction, they take on a state in which, when the extracted toxin is added to a slight scarification

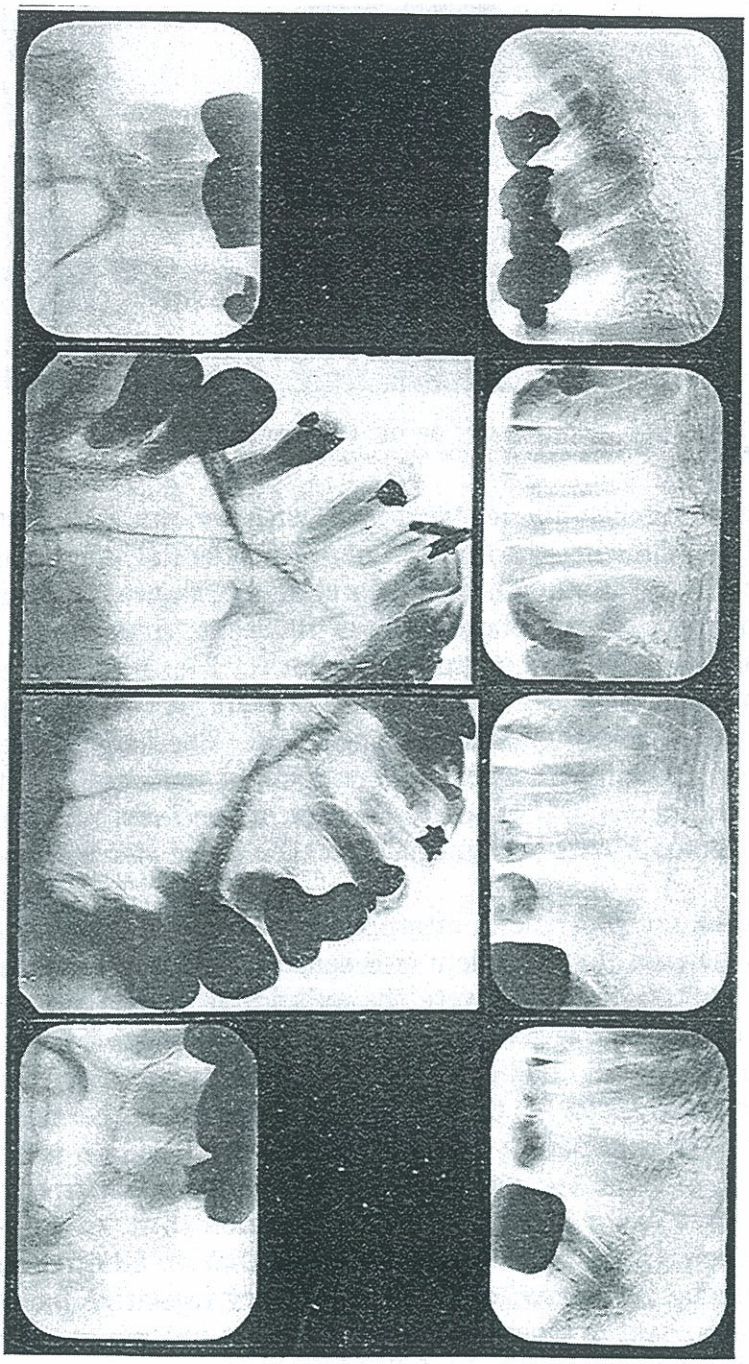


FIGURE 179. ROENTGENOGRAPHIC RECORD OF THE TEETH OF THE PATIENT SHOWN IN FIGURE 178.

of the forearm or introduced in solution into or just beneath the external layer of the skin, there occurs frequently, in a very few seconds, and practically always, in a few minutes, a vascularization with a very marked dilatation of the capillaries. When tubes carrying such a sensitizing antigen are placed beneath the skin of a rabbit, as in its ear, and removed in a few minutes, it is

found that there is a very rapid migration of leucocytes to the zone. Carrell has shown that leucocytes contain an activating substance capable of inducing cell defense and proliferation comparable to the activation of embryo and tissue juice. This suggests as a possibility that dental infections may produce irritations either in the epithelial tissues, as shown in these various skin reaction cases of the preceding chapter, or in mucous membranes, also shown in the preceding chapter; and if, as is frequently the case with these lesions, they remain located in a given spot for a long period of time, it may be possible that a hypersensitiveness, a part of which constitutes a marshalling of the leucocytes, may be one of the important steps in the development of neoplasms. Possibly related to this will be found the development of abdominal cysts, many of which we show produced in rabbits in Chapter 62 of Part Two. In the Chapter on Lesions of the Digestive Tract in Part Two (Chapter 65) we recite a number of cases of lesions of the alimentary canal, chiefly the stomach, which seem directly related to dental infections, inasmuch as chronic lesions, as stomach ulcer which had been recurring for years, have entirely disappeared and have remained absent for a number of years following the removal of the dental infections, and the teeth from which cases, when cultured, produced in rabbits, as shown in those chapters, many instances of stomach ulcer and perforations of the stomach and intestines. We will discuss this phase of this problem further in our general interpretations.

I have said, "*if* she was sensitized." In order to determine this I made extractions from her extracted teeth and tested both of these and also an extract from the organisms grown from her teeth in culture media and found her to react positively to the dermal test and maximum positive in twenty-five minutes, which disappeared in three hours. The same antigen used on control individuals was negative. It is my interpretation, therefore, that she was, as a matter of fact, in a state of allergic sensitization to the toxic substance being developed in her dental infection.

I am quite familiar with the fact that there is divergence of opinion as to whether there is any hereditary tendency associated with cancer; and, indeed, the evidence is far from conclusive that there is such. If, as I have suggested, sensitization processes may tend to contribute to precancerous irritations, it would be entirely possible to explain the association of these irritations in

families without requiring as a premise that the cancerous condition, *per se,* is transmissible. To illustrate: Individuals do not transmit to their posterity, periodontoclasia, or so-called pyorrhea alveolaris. However, it is a condition which is found to involve all the members of some families and be absent in all the members of other families. The factor that seems to be transmissible in this case is an exalted or highly efficient capacity for reaction against the presence of an irritant; and, since all the members of the family have been blessed with this high defense in common, and since all individuals tend to have irritating deposits about the teeth, and irritating food packs about improperly spaced teeth, or those with destroyed contact points, the irritants to which to react are practically universal. The removal of the irritants and prevention of their recurrence will usually be all that will be necessary in these individuals to prevent the development of a local disturbance spoken of as periodontoclasia, or pyorrhea alveolaris. Similarly, since only individuals with a normally high defense reacting against a persisting toxic antigen, seem to develop this state of sensitization, it would not be strange if different individuals in the same family developed such similar reactions to similar irritants. This may be the explanation for the phenomena which are exhibited in the chart shown in Chapter 65 in which it will be seen that the patient has stomach irritation, sluggish liver, and acute digestive disturbance, from which disturbance one of his brothers is also suffering, and also both his father and mother. It is also important that his father's father and one of his father's brothers died of cancer of the stomach at sixty and sixty-three years of age respectively, and his mother's mother of a chronic stomach disturbance, not identified, at the age of sixty-four. The history of this family shows a marked tendency to periodontoclasia in each the patient, two of his brothers, and his father. This, as we have shown, is a disturbance which tends to develop in individuals with normally high capacity for reaction. They, therefore, would also have a high capacity for reaction to other sources of irritation, not necessarily of dental origin, though readily from that source, which might express themselves as sensitizations. If, then, there be an inheritance of a tendency to low defense of stomach tissue, this sensitization process could readily attack that tissue and in this definite but indirect way, either precancerous or cancerous conditions may possibly be associated and related when they occur in different members of the same family, as here shown.

SUMMARY AND CONCLUSIONS.

Since more individuals lose their lives from cancer of the stomach than from cancer of any other type of tissue, and since dental infections are shown in the chapter referred to, to be directly related to so many cases of acute and chronic digestive tract disturbance, we should be exceedingly careful that dental infections are not permitted to become a predisposing factor, for it has been abundantly shown that cancer of the stomach tends largely to develop in the scars of healed ulcers. Until we have more knowledge as to the extent of anaphylactic reactions in the many lesions produced and aggravated by dental infections, we cannot with safety undertake to interpret the full role which dental infections play in acute, chronic, or malignant processes. The evidence, however, is sufficient to suggest extreme caution in matters of prophylaxis.

The evidence available suggests:

(a) That dental infections may produce localized anaphylactic reactions, as irritations of the skin and mucous membranes.

(b) That these sensitizations may develop into precancerous conditions.

CHAPTER XXXII.

RESEARCHES ON DENTAL INFECTIONS AND CARBOHYDRATE METABOLISM.

PROBLEM: What, if any, is the relationship between dental infections and carbohydrate metabolism?

EXPERIMENTAL AND DISCUSSION.

By relating the lesions, which occur in other parts of the body in association with acute and chronic gingival infections, we have an opportunity for securing direct information and also suggestions as to what may be the causative factors producing both the oral and the systemic disturbances. I have shown in Figure 131 Chapter 20 (showing relation of blood chemistry studies to systemic involvements like diabetes, etc.) and also in other places that certain groups of disturbances tend to be associated, as, for example, a pathologically high ionic calcium of the blood, low alkali reserve, low respiratory coefficient, extensive gingival involvement with alveolar absorption, high blood sugar (hyperglycemia), sugar in urine (glucosuria), tend to be associated, and that this group tends not to have deforming arthritis or acute rheumatic group lesions; whereas the group, with the other extreme of divergents from normal, does tend to have susceptibility to the rheumatic group lesions. It is therefore suggested that the associated factors must be operating in these two conditions.

I have, accordingly, undertaken a series of researches to establish, if possible, some of the mechanisms herein involved. Since the presence or absence of sugar in the urine is dependent in diabetes mellitus upon a disturbed carbohydrate metabolism, it is very probable that the mechanism controlling that process is directly related to the various modifications in the two distinct types of lesions. It has been known for some time that the surgical removal of the pancreas always tends to produce typical diabetes with death in the animal, in a few weeks. The rise in the sugar in the blood is constant as it is also in the urine. This has led many investigators to a search for the specific hormones,

which, it was interpreted, must be developed by the pancreas, controlling the metabolism of the carbohydrates. Very erratic but occasionally definite evidence was developed which indicated that the process was a complicated one. Recently Banting,[17] Best, Collip, and Macleod have succeeded by a special technic in isolating a substance from the pancreas, which when injected into normal animals, definitely and rapidly lowers the blood sugar, and which, when administered to depancreatized animals, immediately reduces their blood sugar to, or below normal in accordance with the dosage. They have demonstrated that this substance is a product of the islets of Langerhans. When extracts are made of a whole adult pancreas, a quantity of the specific substance, to which they have given the name insulin, is secured in varying amounts, as judged by the effects upon animals when making injections with this material.

It seems very probable from experimental data that the differences in these reactions are not due entirely to differences in amounts of insulin, but in large part to differences in the amount of some other substance which probably is extracted from the same pancreas, and which excites an influence in the opposite direction. In other words, when carbohydrates are taken into the body they are at first formed into sugars. In a normal individual this sugar is stored in the liver as glycogen and a liberal quantity is carried in the blood to the various tissues of the body where it is oxidized in the process of work and is the principal body fuel. In diabetes the body has lost the capacity for burning this fuel and it accordingly accumulates in the blood. In that state the body has lost the capacity for storing it as glycogen in the liver. Nature also stores away the excess by adding additional carbon, depositing it in the tissues as fat. This fat may be called upon in the absence of fuel, and by oxidizing its carbon atoms from the molecules in pairs, reduces it from fat to glycogen, glycogen to sugar, sugar to butyric acid, and finally carbon dioxide and water. In diabetes the body cannot completely burn up these sugar compounds, does not reduce them lower than a butyric acid, which latter then develops into the acetone bodies which, when they accumulate in the system, become very toxic. In Chapter 64 on Arthritis we record many rabbits in which we have produced typical various types of rheumatism by the injection of cultures from dental sources, usually from patients suffering from rheumatic lesions.

On the theory that the pancreas furnishes two opposing hor-

[17] See bibliography

mones which produce an equilibrium in accordance with their relative amounts, one of which is insulin, I have wondered if it might not be true that another hormone, not as yet isolated, might be one of the substances which is directly attacked and destroyed by the types of infection which produce acute chronic rheumatism; and if in other patients the dental infection or its toxins injures the functions of the islands of Langerhans, thereby diminishing the supply of insulin. It has been shown that, whereas the pancreas of mammals contains two distinct types of secreting cells, one of which constitutes the islets of Langerhans, some of the mammalia have these two tissues separated into different organs, as, for example, in some of the fishes, particularly the scallop.

I have shown in Chapter 20 that cultures taken from dental infections are capable of greatly changing the percentage of sugar in the blood of animals and also the development of a glycosuria, which condition recovered in a few weeks, but which was reproduced in the same animal by reinoculation of a culture from the same patient, which patient was suffering from diabetes. We have, accordingly, repeated this experiment, having in mind especially the structural changes in the pancreatic tissues and in carbohydrate metabolism. We have also undertaken to modify these effects by injecting the animals with the opposing enzyme or hormone, assuming that two exist, which are in apposition in the affects. The results of these studies will be published later. These researches are in progress and have opened up an entirely new approach to a very important problem, since in a large number of our patients there has been a marked improvement in the glycosuria and the hyperglycemia following the removal of dental infections.

SUMMARY AND CONCLUSIONS.

Dental infections may produce marked changes in carbohydrate metabolism and probably structural and degenerative changes in the islets of Langerhans of the pancreas, with the production of hyperglycemia and glycosuria.

CHAPTER XXXIII.

MARASMUS.

PROBLEM: Why do people with rheumatic group lesions tend to be underweight?

EXPERIMENTAL AND DISCUSSION.

Few, if any, of the symptoms of rheumatic group affections are so constantly found as that of marasmus. This condition of progressive wasting and emaciation may range from 10 to 25 per cent in ordinary cases, to 35 to 40 per cent in extreme cases.

The patient shown in Chapter 64 has increased in weight from 72 to 111 pounds, an increase of more than 50 per cent of her weight at the time her dental infections were removed, her normal prior to her affection being about 130 pounds. She had, accordingly, lost nearly half of her original weight. A culture was taken from one of her infected teeth and inoculated into the rabbit shown in Figure 180. In four days' time this rabbit reduced in weight from 1381 to 1105 grams, a loss of 276 grams, approximately 20 per cent. The amount of culture injected was 1 cc. of a 24 hour growth. (Sixteen drops, not quite a teacupful.) B shows the marked tissue atrophy about the eyeball which has shrunken so as nearly to fill the orbit.

It is not, however, necessary that even this quantity of organisms be injected, for even the washings of a crushed tooth will produce this extreme emaciation. A patient presented whose principal lesion was his great emaciation. He stated that he felt fairly well, nothing particularly wrong except that he could not regain his weight, which he was progressively losing. He had several dental infections, largely the result of former pockets of active periodontoclasia, now harboring a mixed infection. One of his teeth was crushed, washed, and centrifuged. The clear solution was inoculated into the rabbit shown in Figure 181. This rabbit lost in weight from 1430 grams to 843 grams, a total of 41 per cent in 16 days. We have estimated by counting the number of organisms and weighing a quantity of them, that the actual organisms inoculated into this rabbit would be approximately one millionth of a gram.

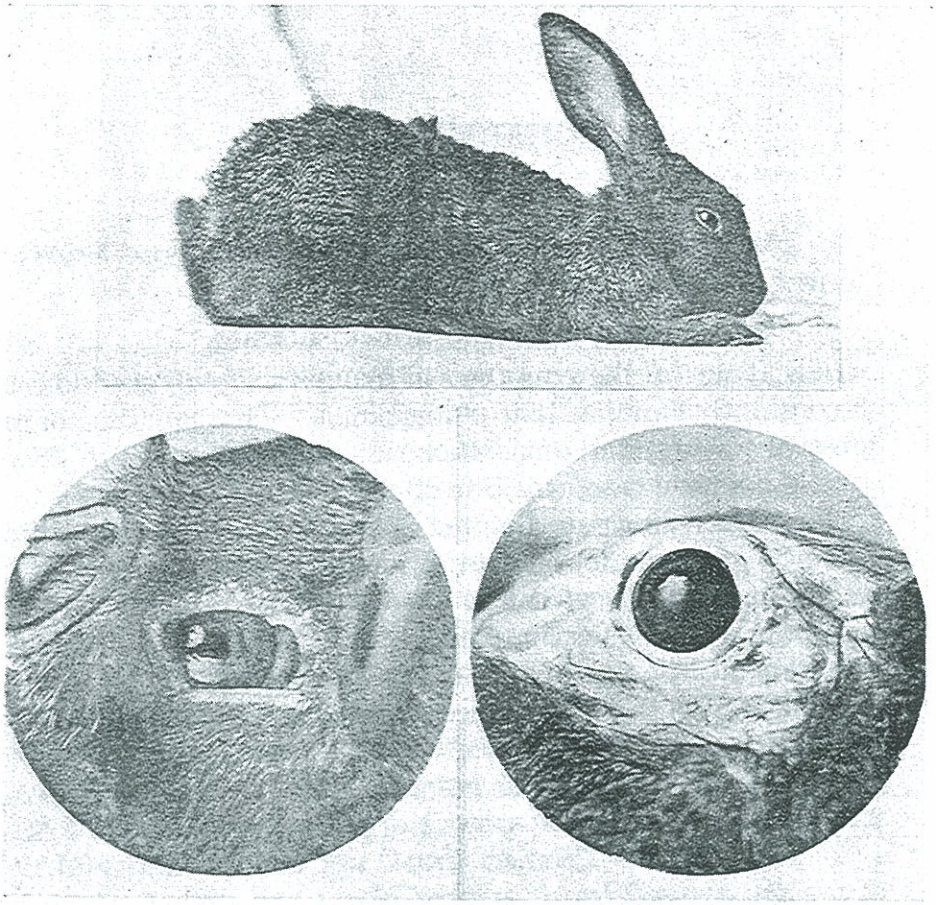


FIGURE 180. MARKED TISSUE ATROPHY PRODUCED BY INJECTION OF A DENTAL CULTURE, TWENTY PER CENT IN FOUR DAYS. NO CLEFT BETWEEN EYEBALL AND SOCKET.

To test this matter still further, we have passed the washings from crushed teeth through a Berkefeld filter and have injected the bacteria-free solutions into rabbits and have produced typical marasmus. We have shown elsewhere, in a discussion of the effects of the toxic substances contained in infected teeth upon experimental animals, that there is a marked loss in weight following their injection. For example, in thirteen rabbits inoculated, intravenously, with filtered washings of teeth, where the death was spontaneous, the average length of life was 5 days, the average loss per rabbit was 191 grams, and the average percentage loss in 5 days was 19, or almost 4 per cent per rabbit per day.

In chapters 59 to 112 there are shown many patients with various types of rheumatic group lesions: muscles and joints,

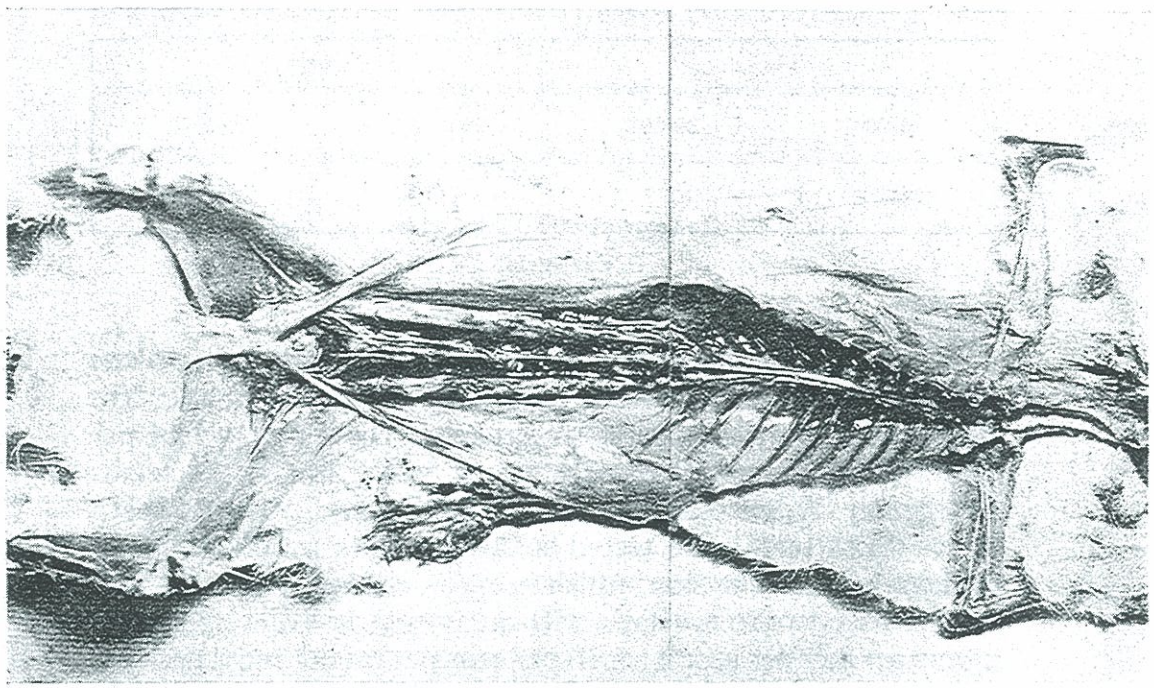


FIGURE 181. TYPICAL MARASMUS IN RABBIT INOCULATED WITH CLEAR WASHINGS FROM CRUSHED TOOTH OF PATIENT. RABBIT LOST 41 PER CENT IN SIXTEEN DAYS.

heart, nervous system, digestive tract, etc. Accompanying these practical cases are shown animals inoculated in various ways with various cultures of dental origin and with toxic substances extracted from teeth, and the percentage of their loss of weight at the time they were chloroformed, or died.

In a group of 667 successive rabbit inoculations, some with cultures and some with filtrates of cultures, and many with filtered washings from crushed teeth, therefore bacteria-free, 33 1/3 per cent, or 220, lost in weight from 10 to 30 per cent in a few days or weeks immediately following the injections; and 8.7 per cent lost from 30 to 50 per cent in weight; 13.6 per cent gained from 10 to 30 per cent, and 3.6 per cent gained from 30 to 50 per cent. It will be seen immediately that, in this group of rabbits selected serially, irrespective of the type of experiment, nature of culture, or method of inoculation, there is a very much larger percentage of rabbits having a loss, than a gain. In other words, 42 per cent of the animals lost more than 10 per cent in weight in a few days or weeks under which they were in observation, extending from that to 50 per cent; whereas only 17 per cent gained

PER CENT LOSS OR GAIN IN WEIGHT AFTER INOCULATION OF 667 RABBITS

Loss		Gain	
10–30%	30–50%	10–30%	30–50%
33.3	8.7	13.6	3.6

FIGURE 182.

more than 10 per cent. (See Figure 182.)

When teeth are planted beneath the skins of rabbits, they often show a loss of weight within 24 hours; and in 100 consecutive plantings for various types of experiments, the loss of weight per rabbit per day amounted to 18 grams, which was 1.4 per cent. In chapter 17, we refer to a strain growing in a patient's teeth six of which teeth were tested on sixty rabbits by planting one of them beneath the skin, which in every instance killed the animals in from two to ten days, with an average loss of weight of 26 grams per day per rabbit, or 15 per cent per rabbit and 2 per cent per day per rabbit, an average total of 205 grams per rabbit. In Chapter 18, we have illustrated two rabbits, full brothers, kept on the same diet, one of which gained continuously and the other began immediately to lose in weight, after being injected with the washings from a crushed tooth.

In this connection it is of interest and important to note that, invariably as the ionic calcium of the blood is reduced by the presence of the implanted tooth, the animals lose in weight. This is clearly shown in the chart in Figure 134, Chapter 20, in which a series of rabbits is shown to demonstrate the changes which take place in the calcium and thrombin of the blood in the presence of dental infection. In these the ionic calcium was very seriously depressed, and, as shown in Chapter 20, the evidence is very strong that this is a fundamental part of the process of bacterial overwhelming. It is also of interest to note, however, that the loss in weight is not exactly proportional to the loss in ionic calcium.

The data, that are rapidly accumulating, strongly suggest, if they do not indicate, that infected teeth contain, in many instances, a toxic substance or substances capable of producing very many grave disturbances in metabolism, only one of which is the universal expression as marasmus. Since it is so common a

symptom of chronic dental infections, that patients having them are underweight and that they tend so frequently to gain in weight after the removal of their dental infections, together with the fact that whether we inject the filtered washings from the teeth or plant an infected tooth beneath the skins of rabbits, this effect generally quite rapidly obtains, we are, therefore, led to the presumption that these toxic substances are directly related to that symptom.

SUMMARY AND CONCLUSIONS.

(1) A study of our clinical records shows that a large percentage of the patients suffering from rheumatic group lesions are from 10 to 30 per cent under weight, and that they tend to return to, or nearly to, their normal within a few weeks or months following the removal of their dental focal infections.

(2) When the same tooth which, when removed, produces such a change in the patient that he or she returns to his or her normal weight, is placed under the skin of a rabbit, it nearly always loses in weight, not infrequently 20 per cent in a few days.

(3) When cultures grown from infected teeth are inoculated into rabbits, whether intravenously, subcutaneously, or intraperitoneally, they tend to lose in weight though usually not so rapidly as when an infected tooth is placed beneath the rabbit's skin.

(4) Filtered washings from infected teeth frequently cause very marked reduction in weight.

We are, therefore, led to conclude:

That dental infections, when they affect the patient systemically, frequently, if not generally, produce a depression of that individual's weight; and that marasmus, whether mild or severe, may be considered one of the diagnostic symptoms in studying the relation of dental infections to general health.

CHAPTER XXXIV

PREGNANCY COMPLICATIONS.

PROBLEM: Do dental infections have a bearing on pregnancy complications?

EXPERIMENTAL AND DISCUSSION.

We have seen in Chapter 21 that one of the conspicuous overloads, which contributes to susceptibility to rheumatic group lesions, is pregnancy; and having noted that so many of our patients either presented with the development of these lesions during pregnancy and lactation, or with a history dating to that period, we were led to study to see whether or not dental focal infections may have an injurious effect upon that state.

It has long been known that the administration of toxic substances to pregnant animals has tended to injure the fetal forms often before the parent was seriously affected. This has been the basis of a procedure for producing a miscarriage by the use of such chemicals as the lead compounds. In our experiments we have found that when infection was introduced into pregnant rabbits, that infection produced more profound effects than when introduced into non-pregnant rabbits, and that this injury expressed itself in fetal forms before it did in the mother. Is it not probable then, that dental infections may have somewhat of the same effect upon human expectant mothers? This is a fact of very great importance in all the campaigns which have to do with the better care of expectant mothers and with the prenatal care of infants, and urges strongly that a part of all government co-operation shall include the placing of the expectant mother's oral cavity in a condition free from focal infections, both for her own safety and for the safety of her offspring.

This is doubly true for the following reason: In pregnancy the demand for calcium is greatly increased, both for the general metabolic processes and for the new fetal form. It has also been shown in the preceding chapters that the presence of the dental infection furnishes a toxic substance which tends to combine directly with the ionic calcium of the blood, and besides produces

FIGURE 183. DEAD FETAL FORMS FOLLOWING INJECTION OF 1CC. OF DENTAL CULTURE.

a toxic factor definitely reducing the available ionic calcium. In practically every instance where a tooth is planted beneath the skin of a rabbit, as we have shown, the ionic calcium of the blood is reduced. If, then, the expectant mother is to be deprived of her available ionic calcium by having its effectiveness destroyed in the circulation, by being attached to a toxic factor, supplied by the dental infection in addition to the increased demand for that ionic calcium, we have two important contributing

factors to a general lowering of defense, to make the third factor more serious and dangerous: namely, the direct injury of the foreign toxin produced by the dental infection upon the fetus. It is not an uncommon clinical experience to have premature labor pains develop with the onset of a dental abscess; and while it is not possible, in a given case, to say what the relative importance of different contributing factors has been, it is not improbable that many miscarriages or prenatal injuries, many of which latter are permanent, may have their origin directly in the obscure and unsuspected dental infections.

We, accordingly, injected cultures from dental origin into pregnant rabbits similarly as in our other studies. Figure 183 shows a dissection of such a rabbit, in which five nearly developed fetal forms are dead and undergoing decomposition from the injection into the ear vein of 1 cc. of a 24 hour growth of a culture from a tooth.

As a further means of study of this problem, we have planted pieces of infected teeth beneath the skin of pregnant rats in order that we might, if possible, observe the effect on both the mother and the offspring. The period of gestation in rats being three weeks, makes a very short experimental period, and it is difficult to determine the progress of the period of gestation by the appearance of the animals. There has been evidence of the premature birth of the offspring within a couple of days after the planting of the piece of infected tooth.

SUMMARY AND CONCLUSIONS.

We would, therefore, summarize these studies as follows:

(1) These researches have shown that, in animals, infections from dental origin may have a very far-reaching effect on both the expectant mother and her fetus, which latter may be prematurely expelled or may be rendered lifeless.

(2) Inasmuch as a large number of our serious cases of rheumatism, heart, and kidney involvements, have their origin at the time of pregnancy in humans, in which cases our clinical histories show that there have been present extensive dental focal infections, it is suggested as important, if not imperative, that expectant mothers shall be free from dental focal infections, both for their own safety and efficiency and for the continued vitality of the fetus.

CHAPTER XXXV.

SPIROCHETE, AMEBA, AND OTHER NON-STREPTOCOCCAL INFECTIONS.

PROBLEM: Do other organisms than streptococci enter the human system through dental infections?

EXPERIMENTAL AND DISCUSSION.

The conclusion that has been reached in nearly all the recent reports on dental infections, bears out the evidence in the preceding chapter, to the effect that, in general, dental infections may be considered as streptococcal or diplococcal infections. Our studies are revealing that while dental infections are practically always a part, and usually the all important part of the involved microörganisms, there are present with the streptococci, frequently, other types of microörganisms which have a very serious effect on the host. These may include either protozoa or bacteria or both. We would discuss two of the protozoa infections first.

In Figure 184 we have a large abscess on the neck which had resisted treatment for many weeks. A bacterial examination of its contents, shown in B, disclosed a large number of amebæ. The history of the case revealed that a lower left first molar had abscessed with a fistula developing below the mandible, which later developed into a chronic abscess which persisted after the extraction of the tooth. C shows the mandible where the tooth was extracted. The use of succinimid of mercury, a good amebacide and disinfectant, as a wash and pack, produced the immediate healing of the abscess.

We do not know to what extent spirochete forms from the mouth enter the human body. We are coming to believe that they do so much more often than has been realized.

Figure 185 shows a rabbit's knee which has developed a huge tumor-like mass which, when opened, proved to be almost pure culture of spirochetes. A shows a large abscess in the thigh of the rabbit, from which a nearly pure culture of spirochetes and fusiform was obtained, as shown in the smear in Figure B. The rabbit was inoculated intraperitoneally with the washings from a periodontoclasial tooth of a patient who had been suffering from

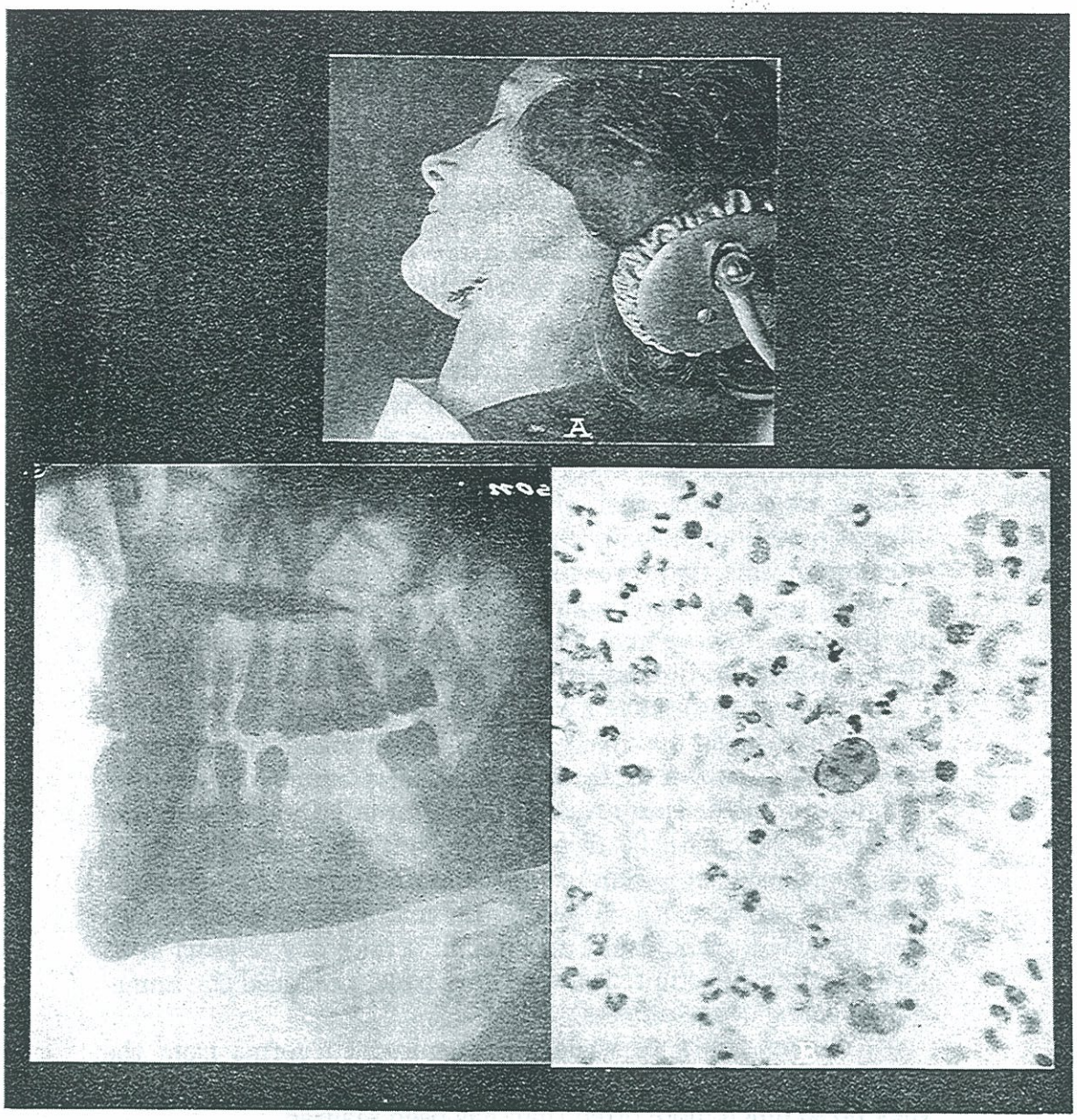
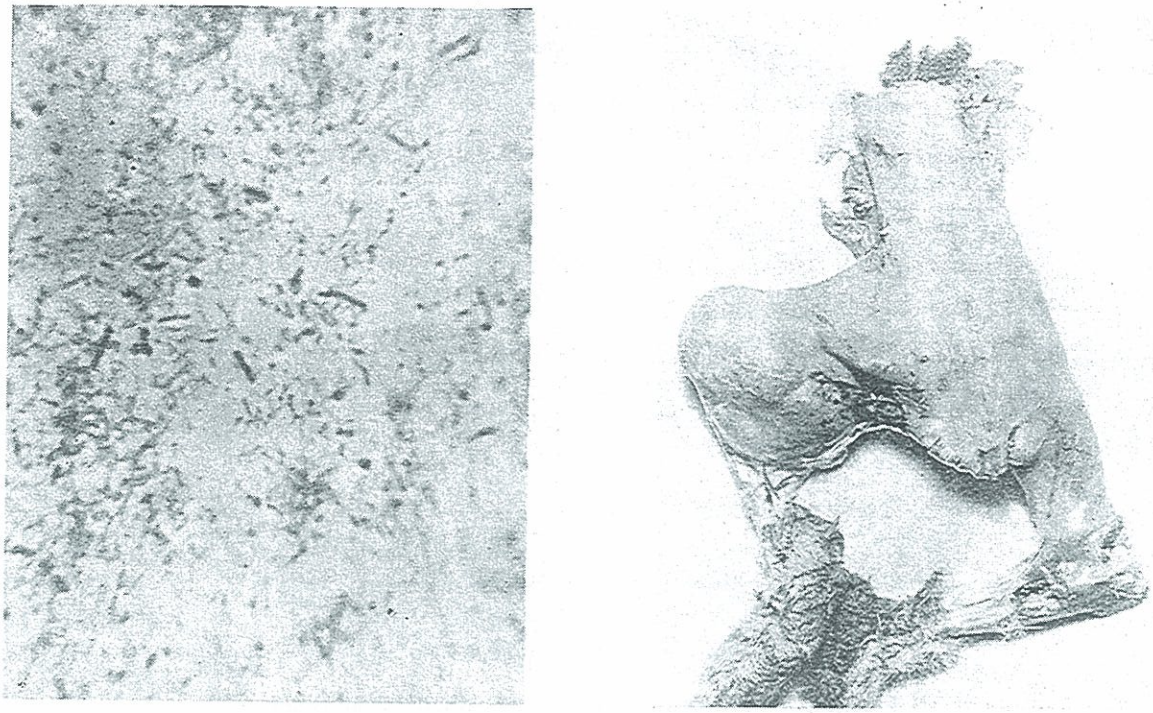


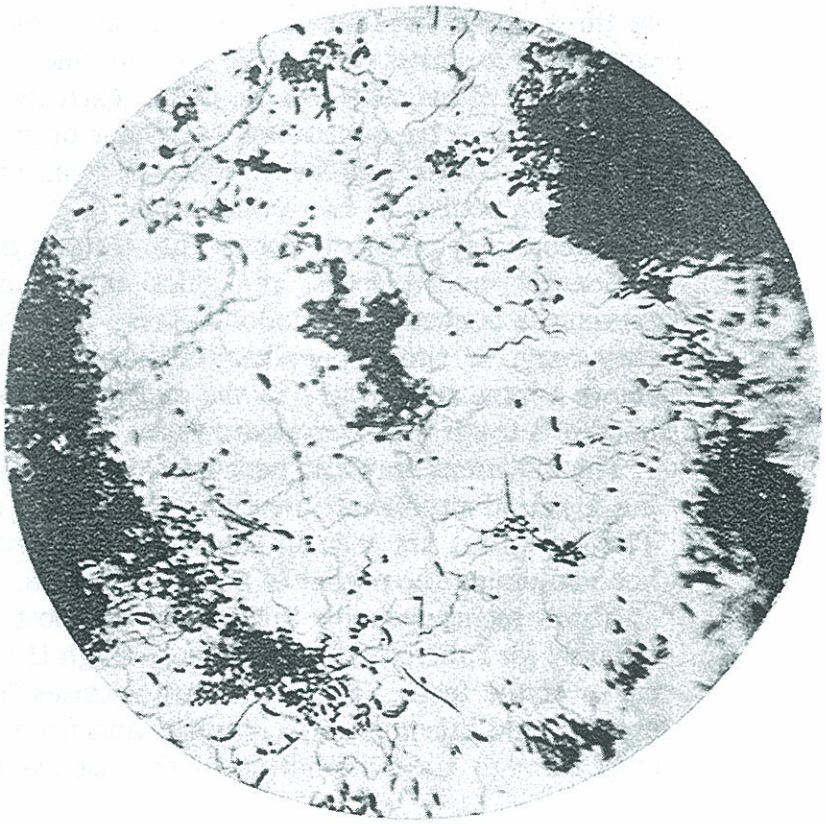
FIGURE 184. ABSCESS ON NECK SHOWN IN A; AMEBA INFECTION SHOWN IN B; ORIGIN FROM INFECTED TOOTH SOCKET SHOWN IN C.

an unusual type of neuritis, which was completely relieved by the extraction of the involved tooth. The lesion in this rabbit's thigh contained a culture, apparently, presumably like the culture which we had studied in the pocket beside the tooth before the extraction of the tooth.

The direct influence of the spirochete infections upon the health of the individual may be both severe and rapid. Such a case is shown in Figure 186. This man had lost eighteen pounds in weight



IGURE 185. SPIROCHETAL ABSCESS DUCED IN RABBIT IN A; B, CULTURE AME.



IGURE 186. CULTURE OF SPIRO-TES FROM TRENCH MOUTH, WHICH SED PATIENT TO LOSE EIGHTEEN NDS IN THREE WEEKS. WITH LOCAL ATMENT HE GAINED TEN POUNDS IN) WEEKS.

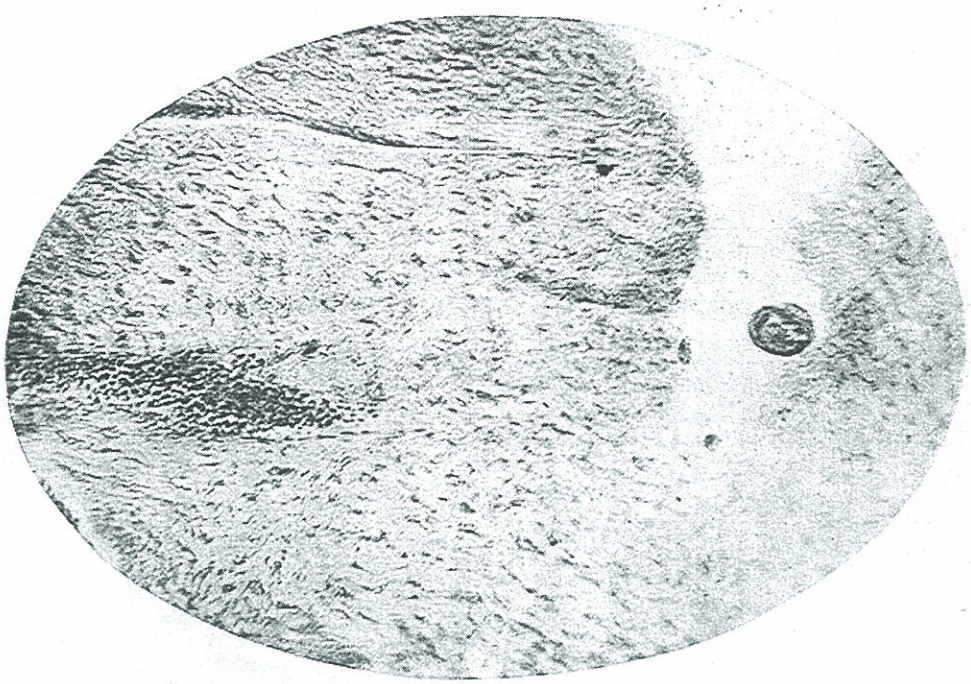


FIGURE 187. AMEBA INFECTION DEEP IN THE GINGIVAL TISSUE.

in three weeks' time, and a most thorough medical examination could find no other cause. As an experiment, as well as a wise procedure, in his case because of the extreme painfulness of his gums, the first treatment was by means of packing the selected germicides between the teeth, with the remarkable result that he gained ten pounds in two weeks' time.

Amebæ may penetrate deeply into the soft tissues surrounding peridental involvements, and since amebæ are nearly always present in pockets of periodontoclasia, it is not improbable that they may, at times, penetrate far into the tissues. Figure 187 shows a large ameba deep in the gingival tissue in the neighborhood of a tooth with periodontoclasia.

The infections may also penetrate deeply into the bone adjoining a periodontoclasial infection. Figure 188 shows such a case. The organisms are seen in the haversian canal of the alveolar bone adjoining the pocket of periodontoclasia.

It now seems probable that one of the most important portals of entry for tubercular infection is through the cavities of dental caries of the teeth. From the dental caries they penetrate the exposed and infected pulp chamber, and from this gateway proceed through the lymphatics to the deep and cervical lymph

FIGURE 188. ORGANISMS IN AN HAVERSIAN CANAL, ADJOINING A PERIODONTOCLASIA POCKET.

glands of the neck. Careful observers in dental practice are constantly seeing the phenomenon of enlarged cervical glands, that have been persisting for periods of time, disappear with the removal of infected teeth. Particularly is this true with undernourished children and their carious deciduous teeth.

Another important phase of this problem is the role of dental caries and the teeth, in the matter of the furnishing of a nidus of infection, which come to be carriers. Particularly is this true of such diseases as scarlet fever and diphtheria. A first requisite for the disinfection of carriers of this type involves a complete eradication of dental infection and dental caries.

But there is another type of infection which is very important and has to do with those involvements, which express themselves through long periods of the individual's life, as recurrences of a one time active process. A typical illustration of this is the following. A patient who had suffered for years from malaria went to a mountain climate to escape the possibility of the mosquito infection; but notwithstanding that she had gone to a malaria free

district, she had frequent and definite recurrences of her malaria infection. She returned to Cleveland in midwinter, and in the process of my making her safe from her dental infections by the elimination of foci, after the extraction of her first tooth, she developed a violent and typical attack of malaria fever which was positively diagnosed by finding the plasmodium in her blood. There seems no doubt but that the stirring up of this nidus set free again into her system this organism to produce its cycle. A most remarkable part of her history has been that, whereas these recurrences of malaria had been frequent prior to the removal of her dental infections, she has not had a recurrence in the five years since the removal of them.

It is not yet clearly established whether lethargic encephalitis is produced by an organism of the diplococcus streptococcus group, or by a filterable virus. However, there have been many investigations reported which have tended to establish that it is due to the former. In Part Two on Degenerative and Deficiency Diseases, Their Relation to Dental Infections, I discuss in detail a case of lethargic encephalitis in which it seemed very probable that we were dealing with a type of infection in the tooth, which was directly related to that clinical syndrome, where the tooth was taken from a patient suffering from that disease. In this connection I will state that one of these teeth from this patient placed beneath the skin of thirty different rabbits, produced death in from a day and a half to six days, with one very large rabbit living ten days, and the culture from which tooth, when injected subdurally, produced symptoms strongly suggestive, if not typical of that disturbance. It is also significant that three other teeth taken from this same patient produced similar effects.

The seriousness of these spirochete infections, when they become acute, is common to all practitioners who have had an opportunity for large experience and are generally referred to as Vincent's angina, trench mouth, etc. They may, or may not, show many fusiform. Frequently they are practically pure strains of spirochetes. We will discuss these in their different types and classifications in Volume Three on Diagnosis, Prognosis, and Treatment.

SUMMARY AND CONCLUSIONS.

(1) Our experience with these and other cases suggests to us the great need for very careful study to determine whether or not,

particularly in cases of extensive periodontoclasia, there is an invasion of the organisms of those infective processes, and whether the sensitization reactions discussed in Chapter 30, are not directly produced, in many cases, by toxic substances generated by these other types of organisms.

(2) The evidence at hand strongly suggests that infected teeth are the harbingers of both contagious and infectious organisms which may either attack the host on recurring occasions, or may be transferred by the host who may be non-susceptible and simply a carrier, to susceptible individuals.

(3) Dental prophylaxis becomes imperative both for the safety of the individual and for the community in which he lives.

While the streptococcus seems universally to be present in dental infections in practically all cases of systemic involvement, in addition to this variety the evidence seems to establish that each staphylococci and spirochetes may pass from infected teeth to other tissues and proliferate in localized areas; and, similarly, that when certain mixed strains are injected into experimental animals, localized spirochete infections may develop in their tissues. Systemic involvements from spirochete infections and their localization in experimental animals are, however, relatively rare.

CHAPTER XXXVI.

NUTRITION AND RESISTANCE TO INFECTION.

PROBLEM: Does faulty nutrition, through a deficiency diet, decrease the defense against dental infections?

EXPERIMENTAL AND DISCUSSION.

Few of the overloads so effectually destroy the defense for infection and to such a degree, as does disturbed nutrition. It has been the universal history of the world that wars and famines have been followed by devastating infections. The recent newer knowledge of the nature of foods and their effects upon the developing structures has enormously widened our knowledge of nutritional disorders. The epoch-making work of McCarrison in India, the Melanbys in England, McCollum, Funk, Mendel, Hess, and many others in America, has rapidly established the role of deficiency diets in the long list of physical affections which are more or less common in all lands; and various types of lesions are shown to be very clearly dependent upon the absence of sufficient quantities of accessory food factors, generally spoken of as vitamins A, B, C, and D. McCarrison, particularly, has shown that many of the same diseases can be produced either by deficiency diets or by inoculation with certain infections.

In our extensive studies of the reactions on animals inoculated with different strains of dental infections, we have repeatedly produced symptoms and lesions which resemble in a marked degree those produced by deficiency diets. This research was established to assist in determining the effect of diet in destroying the normal defense of animals and the extent to which the development of infection processes has entered into the clinical pictures of nutritional disturbance, to produce the lesions that are found. Figure 189 shows three views of two rats, same age, one kept on normal diet, and the other on a diet deficient in vitamin B. It is shown here partially paralyzed from polyneuritis, which characterizes the deficiency of this vitamin. It would certainly be expected that animals with nervous systems undermined by this deficiency of feeding would be more sensitive to infection introduced into the animals' bodies. Figure 190 shows

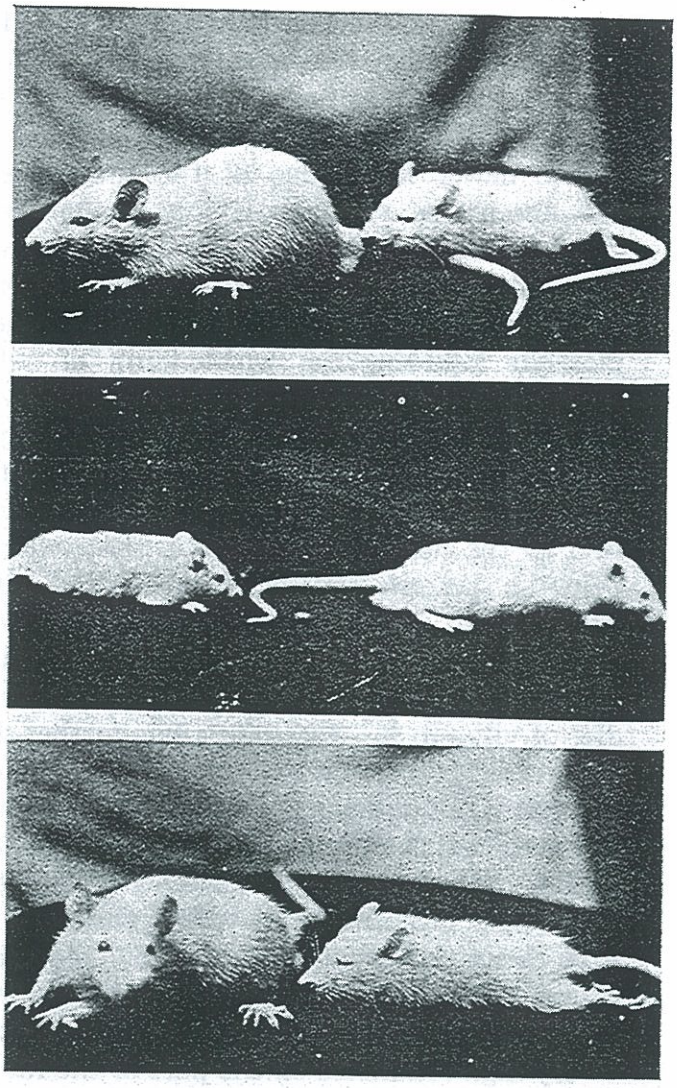


FIGURE 189. TWO RATS SAME AGE, ONE ON NORMAL DIET AND THE OTHER DEFICIENT IN VITAMIN B.

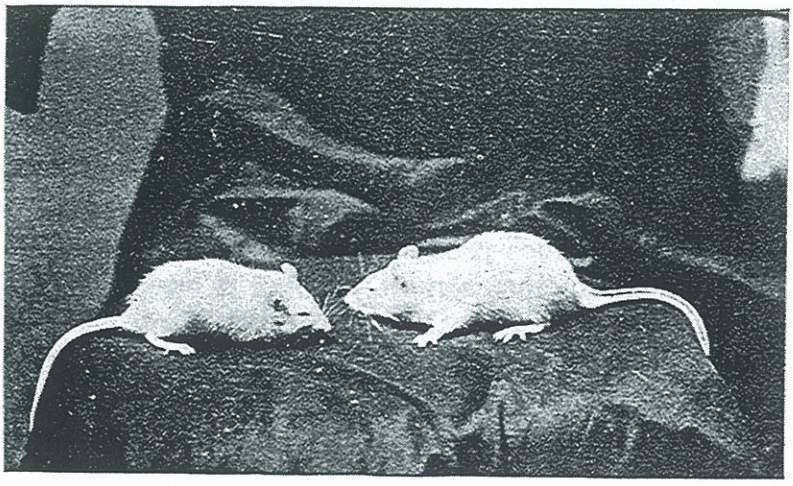


FIGURE 190. THE RATS ON THE DEFICIENCY DIET HAVE ALSO LESS RESISTANCE FOR INFECTION.

two rats, same age, one on deficiency diet, and the other on normal diet, both of which were inoculated with the same quantity of a strain of dental infection and in which a dose one-third of the tested lethal dose for a normal rat was used.

The newer knowledge of the specific lesions produced by the absence of vitamins A and B has revealed that certain changes in the elements of the blood are in evidence before the physical disturbances appear. Cramer, Drew, and Mottram[18] have shown a progressive decrease in the number of blood platelets following the withholding of vitamin A, resulting in a marked thrombopenia which, they state, is the only constant lesion in deficiency of this vitamin, just as lymphopenia is characteristic of deficiency of water-soluble B. They have also shown that the defense to infection is largely in proportion to the number of platelets, that, when they are reduced below a certain critical number, the animals become an easy prey to infective conditions which develop spontaneously, and which may give rise to secondary anemias, but which disappear, if the condition has not gone too far, on the addition to the diet of vitamin A. McCollum has further divided vitamin A, as understood previously, by limiting its classification to the specific substance, the absence of which produces xerophthalmia. He has characterized as vitamin D, the fat-soluble factor, the absence of which produces the lesions classified as rickets.

We have inoculated rats with given amounts of culture grown from dental infections to determine, if possible, whether in that animal the absence of the vitamins would make them more susceptible to this infection. These results have tended to disclose a very high resistance on the part of the rat for streptococcal infections. We have, however, noted in our inoculations of rabbits that in many instances there was a marked decrease in the platelets and in the thrombin as the result of the streptococcal inoculations, which effects in a degree are as extreme in some instances as the withholding of the specific vitamins.

Vitamin B has been shown by Cramer to be directly related to the production of lymphopenia. Similarly, we have found strains which produced a very marked lymphopenia in animals, whereas other strains produce a very marked lymphocytosis. These are illustrated in the blood counts shown in the chapter on hematological changes in the blood produced by dental infections.

An important phase of nutrition is involved in the typograph-

[18] See bibliography.

ical climate and isolation of various communities. I shall not enter into a discussion of this problem of nutrition in its relation to localized community conditions. This has been done extensively by such writers as McCollum, McCarrison, etc. I will, however, report the result of a special study that I made among the mountaineers of North Carolina. In these studies, in which I went from home to home on the mountains and also in the valleys, and made tabulations, I found abundant evidence that deficient nutrition was increasing the susceptibility to the rheumatic group lesions. The diet of the mountaineers at that time (Feburary and March, 1919) consisted largely of fat pork, coffee, and the separated grits of the white corn, with a more than liberal use of tobacco, chiefly as snuff, which is painted around the teeth and consists of the powdered stems and leaves. This was far from being a balanced diet. Many of the individuals went for months without milk in their diet, and green foods and vegetables were practically unknown out of season. These individuals showed, in many ways, distinct symptoms of calcium starvation. They were underweight, nervously irritable, and aged young, being frequently more decrepid at fifty to sixty than they should be at seventy to eighty. The most striking feature, however, was the very marked prevalence of rheumatic group lesions, and in many homes I found bedridden sufferers with endocarditis, acute rheumatism, recurring, chronic arthritis, and many cases of digestive and nervous system disturbances. A more careful study of these individuals revealed a very unusual prevalence of dental caries, with striking illustrations of large numbers of broken down teeth, and hence with putrescent pulps and apical involvements, and yet, these frequently existed without fistulæ or evidence of a normal defense and a reaction. They were not maintaining local zones of quarantine about these infected teeth or they could not have been in this quiescent condition.

In order to throw some additional light on the problem as to whether or not dental infections are more injurious in individuals on deficiency diets, I have undertaken to reproduce the conditions in animals for study. Different groups of rabbits and rats have been placed in a condition of deficiency in nutrition and then subjected to inoculations and implantations of infected teeth, to determine whether or not those with an unbalanced diet are more susceptible to the infections than the normals. The evidence to date, while, in general, corroborating this viewpoint, does not

justify, however, the conclusion that the lowered defense can be charged in large measure to deficiency diet. In many instances the animals with deficiency diet showed remarkable power of defense against infection, though not quite equal to the normals. The results, in general, have been a disappointment in that they have not thrown as large a responsibility on the diet as we had expected. These studies are being continued and will be reported in extended detail later.

The researches on this problem have been in progress approximately a year and the data are being accumulated, which should throw dependable light on this important problem. Rats have not proved to be a suitable animal in which to determine variations in streptococcal defense.

SUMMARY AND CONCLUSIONS.

The data at hand suggest:

(1) That the effects of variations in the diet do not express themselves quickly in specific defense.

(2) That variations in diet by the limitation of various vitamines produce effects which, in general, are similar to those of overload.

(3) Deficiency diets, particularly disturbances resulting in a calcium hunger, tend directly to lower the defense to dental infections.

CHAPTER XXXVII.

THE RELATION OF THE GLANDS OF INTERNAL SECRETION TO DENTAL INFECTIONS AND DEVELOPMENTAL PROCESSES.

PROBLEM: To what extent are the glands of internal secretion related to dental infections and to dental developmental processes?

EXPERIMENTAL AND DISCUSSION.

Probably no department of modern medicine has had a more rapidly developing literature than that of the glands of internal secretion. It is also true that a great deal that has been written has been based upon insufficient experimental evidence, being largely surmises as to the probable role of these various glands. There can be no doubt, however, of the important part which these glands play in all the vital processes, including calcification, metabolism, and immunity. I will not undertake to give an historical review of the literature in its relation to dental problems, as it would be much too voluminous for insertion here. (Its bibliography alone would cover at least one hundred pages.)

I have directed these researches chiefly along the following lines:

(1) The Correction of Disturbances and Disfunctions of the Glands of Internal Secretion of the Patients by the Removal of Their Dental Infections.

(2) The Production of Disturbances in the Glands of Internal Secretion of Animals by the Injection into Their Circulation of Cultures Taken from Teeth of Involved Patients.

(3) The Modification of the Patients' Systemic Involvements from Dental Infections by the Administration of Extracts of These Glands.

(4) The Improvement of the Functioning of the Glands of Internal Secretion by the Mechanical Stimulation Induced by the Movement of the Bones of the Face and Base of the Skull.

We will discuss these under these four heads.

1. THE CORRECTION OF DISTURBANCES AND DISFUNCTIONS OF THE GLANDS OF INTERNAL SECRETION OF THE PATIENTS BY THE REMOVAL OF THEIR DENTAL INFECTIONS.

It is difficult to state which of these glands is most frequently involved. Some are very frequently involved, particularly the thyroid and ovaries. In this great belt lying along the Great Lakes, there is exceedingly little iodin available in the soil and water, and, as a result, thyroid involvements of the various types are very common. It has, accordingly, become necessary to provide iodin for the girls of all this district to make up for this deficency.

Individuals with a defective thyroid due to lack of iodin, readily have that slight disfunction very greatly disturbed and aggravated by dental infection; and the dental infection is distinctly less disturbing to this gland, in the presence of this ample iodin in the food. For example, thyroid involvements from dental infections apparently are very much less frequent among peoples living along the oceans where the spray is drifted inland by the winds, than in this Great Lake belt.

It is now understood that girls are very much more liable to have thyroid involvements than boys, so much so, that the latter are practically free from them unless it be a condition carried forward from the time of a prenatal insufficiency of the mother. Girls and women tend to have the thyroid involvements develop during the periods of physical stress, particularly during puberty and pregnancy. At these times it is very important that they should have an additional supply of iodin if this is not supplied in sufficient quantity in the food. A few grains given every six months will be sufficient to retain the normal functioning of the thyroid.

To test out this important discovery, Marine and Kimball got permission to administer iodin twice a year to the girls of the public schools of the city of Akron, only those being accepted who furnished from their parents or guardians a written request for this treatment. Kimball[19] in his report entitled "The Prevention of Simple Goiter in Man," published in the American Journal of Medical Sciences, May, 1922, No. 5, summarizes the results as follows:

There were 2305 girl pupils included in the tabulation of those not taking treatment and 2190 in the tabulation of those taking treatment. All were examined every six months and very care-

19 See bibliography.

ful records maintained. They divided their findings into three groups: First, those girls who had normal thyroids. Of these there were 906 in the group taking treatment and 910 in the group not taking treatment. In the group taking treatment only 2 or 0.2 of one per cent developed goiter; whereas in the group not taking treatment 347 of the 910 developed definite enlargement of the thyroid, or 27.6 per cent.

Of those with a slightly enlarged thyroid, there were 477 in the group taking treatment, of which only 3 were recorded as having the goiter increased; whereas, in those not taking the treatment, there were 127, or 13.3 per cent where the goiter was increased. Similarly, of those with slightly enlarged thyroids, 659 of those taking treatment were recorded as having a decrease in the size of the goiter, whereas in those not taking treatment only 134, or 13.9 per cent, showed decrease.

In the group with moderately enlarged thyroids, of those taking treatment there were 29, or 20.3 per cent, showing no change; and of those not taking the treatment, 57, or 64 per cent. Of those taking treatment none were recorded as having an increase in the size of the thyroid, where it had been recorded as moderately enlarged to begin with, while in those not taking treatment 21 of this classification showed enlargements, or 23.6 per cent. But even more striking is the evidence of therapeutic effect; for in this group with moderately enlarged thyroids of those taking treatment 114, or 79.7 per cent, showed a decrease. There is, therefore, strong evidence that the administration of the iodin had both a very marked prophylactic and therapeutic effect.

Since the publication of this practical test developed by Marine and Lenhart in their intensive researches, the procedure has been carried out in a great many countries as well as many districts of this country, and practically always with the same most gratifying results. With regard to the possible ill effects Kimball reports that, in all the cases taking the prescribed two grains of sodium iodide twice yearly, there was not a single evidence of exophthalmic goiter nor any evidence of a nervous irritability simulating it; and in all the cases only 11 of iodide rash, 6 of which were so mild as not even to require treatment. Less than one-half of one per cent showed any lesion or evidence of disturbance from the treatment. The importance of this cannot be overestimated since in many districts, such as the glacial areas of Switzerland, Alaska, and British Columbia, a very large percentage of the humans and animals suffer from endemic goiter, and both are equally easily controlled, results being practically complete; and

goiter is now considered one of the easiest of the known diseases to prevent.

The result of this practical test of the value of new facts brought out by laboratory experimentation has been that the children in many inland communities in America and all children in Switzerland are compelled by law to be given the iodin at regular periods. If space permitted, it would be of interest to refer to other phases of the role of iodin in thyroid functioning and general metabolism. Two others will be sufficient.

Animals are often involved as are humans. In a district of British Columbia where the iodin is particularly scarce in the soil and therefore in the plants and foods, it was found impossible to raise hogs because the young had little or no hair, had rough scrofulous skin, and failed to develop properly. The administration of a few grains of iodin to the pregnant sows, completely corrected the condition, so that now the raising of hogs in that district is carried on with as great ease and perfection as in normal communities. The humans in this district were also seriously affected.

Similarly, the fish in a hatchery of a neighboring state were dying off at such a rapid rate, that it seemed necessary to abandon the entire enterprise. At the suggestion of Dr. Marine who found on examination that these fish were suffering from goiters, they were given iodin in their food. This completely cured the malady.

It is a very frequent experience to find acute thyroid involvements subside rapidly and often apparently completely with removal of dental infections. In Chapter 60 I have discussed in detail such a case. It is of particular interest first because the systemic symptoms cleared up very completely and the local thyroid enlargement reduced approximately to normal. Two years later with the development of an apical involvement of another tooth, the symptoms returned similarly, and if possible, more severely than at first, since there was a very considerable heart involvement, as tachycardia; and after the removal of this infected tooth the symptoms and the activity of the thyroid both disappeared. This condition of disfunction of the thyroid is so frequently met in our clinical work, that we look upon it as one of the very common systemic expressions of dental infections.

In the above chapter I refer to several cases with a discussion of the clinical phases, which illustrate clearly, without repetition here, that the removal of the dental infections in a large number

of these cases completely relieves the acute disturbance, and the thyroids return to an approximately normal functioning, and otherwise very grave symptoms disappear. In that chapter on Endocrines I also discuss the thymus and parathyroids.

In further study of the improvement in functioning of glands of internal secretion by removal of dental infection, I will discuss the effects of dental infections on ovaries and testicles. A causative factor frequently associated with infections of these glands is an infective process which, because of the nature of the tissues involved, induces individuals suffering from such disturbances, to suffer in silence, notwithstanding their knowledge that there has been no opportunity for such an infection. In the chapter on Primary and Secondary Sex Organs I recite the details of a number of cases where the evidence seemed very strong that the dental infections were the primary factor in involvement of these tissues. A brief review of some of these is as follows:

A uterine discharge thought to be malignant in origin, which had persisted for six months and was growing progressively worse, entirely disappeared and has not returned for two years by the removal of dental infections, illustrated in a figure of Chapter 62. A young woman, typical of many, suffering from a very severe suppression at the time of her periods, accompanied by marked mental disturbance, was completely relieved by the removal of dental infections. The condition, however, returned, and the removal of further dental infection completely corrected the trouble without return for a year and a half. A man with a painful swelling of the testicles had the condition greatly relieved by the removal of dental infections. All of these cases are further discussed in succeeding paragraphs under the heading of the Production of the Disturbances in Animals by the Inoculation of Dental Infections from Involved Patients.

While it has been known for some time that the pancreas plays a very important role in the metabolism of carbohydrates, the proof that the Islets of Langerhans furnished an internal secretion capable of correcting this disturbance, has not been available until the epical work of Banting, Best, Macleod, etc., through the isolation of insulin. When this substance is injected into normal animals, there is an immediate reduction of the blood sugar; and, similarly, when injected into animals from which the pancreas has been removed and which have thereby been induced to develop typical diabetes, the blood sugar is reduced in accord-

ance with the dose of insulin injected. While it has been known that the pancreas plays this important role in the development of diabetes, it is not known what factors have been most active in causing this disturbance of the pancreas.

In the course of these researches on The Relation of Dental Infections to Systemic Disturbances, many important new facts have been developed through the study of the chemical changes in the blood. Among these the changes in the blood sugar, due to the removal of dental infections, has been a very important one. A group of these cases is shown in Figure 131 of Chapter 20.

A first effect of the disturbance of dental infections in cases of hyperglycemia is an aggravation of disturbance regardless of the method of conducting the surgery. These patients are poor risks for surgical operations, whether in the mouth or elsewhere. In another chapter I speak of the serious effect on these patients of the use of adrenalin. Since adrenalin is capable of producing in individuals or in animals an increase in blood sugar, or a lowering of the rate of metabolizing of carbohydrates, its injection with the anaesthetic, as is common practice with novocain to produce a more prolonged anaesthesia, frequently causes a very sharp rise in blood sugar in patients already suffering from a mild hyperglycemia, and an alarming rise in patients with a severe sugar retention. It is, of course, obvious that in these patients the use of adrenalin must either be entirely dispensed with or reduced to a minimum.

In ordinary dental practice diabetics are frequently presenting for service, who do not themselves suspect such a condition; and except he be trained in the methods of diagnosis, the dentist will rarely suspect the condition unless the patient has informed him. In our clinic where we make very frequent chemical analyses of the blood as part of our research, we find a large number of patients with a mild or even severe diabetes mellitus who have no suspicion of the condition. Nor is an analysis sufficient for establishing the presence of a diabetes mellitus, since there may be either an abnormal condition of the kidney, which allows sugar to pass from the urine into the blood even though the blood sugar is not up to the threshold of danger, or the sugar may be above the threshold in the blood, and not be present as a glycosuria. We do not consider that the reduction in blood sugar is of itself sufficient evidence to justify the conclusion, that the pancreas has been injured by the presence of dental infections, even though

carbohydrate metabolism is definitely improved by the removal of dental infections. We would, accordingly, wish to consider the data in this paragraph in connection with that in the next section on the effects on animals.

II. THE PRODUCTION OF DISTURBANCES IN THE GLANDS OF INTERNAL SECRETION OF ANIMALS BY THE INJECTION INTO THEIR CIRCULATION OF CULTURES TAKEN FROM TEETH OF INVOLVED PATIENTS.

It is very significant that in the inoculation of over 1500 rabbits with cultures from dental sources taken from patients suffering from various disturbances, it is exceedingly rare that the glands of internal secretion are directly invaded by organisms, unless the patient from whom the dental infection was taken was suffering from an active process. This does not mean that all animals inoculated become so infected; nor does it mean that this becomes of necessity a competent method for diagnosing whether or not the patient has such an involvement. In the chapter on Elective Localization of Organisms, I have showed that the quality of elective localization is directly related to the culture medium furnished by the patient, and that a patient, with a diseased organ tends to furnish a modified culture medium, which in many instances seems to develop in the organism an elective localization for that tissue. We are not able to determine the completeness of the vicious cycle: namely, the role of the organ, furnishing to an individual with a disturbed general defense, a toxin and bacterium which attacks the involved tissue already injured by some other cause, which diseased tissue furnishes some substance to the blood stream which develops or seems to induce in the organisms an affinity for that particular tissue. That this quality is transient in the organisms we have showed by the fact that, when they are grown on artificial media for a short time they tend, usually, to lose this elective localization quality; but that it is specific to a degree in the organism during the immediate period following its transfer from the dental infection of the patient suffering from that lesion, to an animal without a lesion in the similar tissue, where it tends to develop disturbances in normal tissue of the type of that which is diseased in, or invaded by, infection from the dental infection of the patient.

To save repetition of illustrations we do not present here many of the reproductions of these lesions in animals, of which a large number of cases are shown in the chapters on Primary and Secondary Sex Organs and Endocrine System. Briefly these results

show as follows: In the case shown in Figure 148, Chapter 22, four female rabbits were inoculated with the culture taken from the teeth of a girl suffering from acute ovarian involvement, and all four developed infection of the ovaries and tubes, or 100 per cent; whereas, in the total number of fifteen hundred rabbits inoculated, of which approximately half are females, this involvement has not been recorded in one per cent of the females. In the case referred to under the previous heading with purulent uterine discharge one of the rabbits inoculated developed an acute infection of the ovaries, tubes, and uterus. In the case shown, illustrating the patient suffering from pain and swelling of the testicles, three rabbits were inoculated with cultures from three different teeth. All three developed, as shown in illustration of same in Part Two, acute infection of the testicles; whereas, in approximately 750 male animals inoculated with cultures taken from dental sources, not one per cent has shown involvement of these tissues.

A typical illustration is shown in a figure of Chapter 62 in which case the patient had suffered from an ovarian cyst which was removed eight months previously and was approximately the size of a goose egg. Five female rabbits were inoculated with the culture from her extracted tooth and two developed cysts of the ovaries. Two of these are shown in Figure 191. One has three small cysts on each ovary. The rabbit was posted too soon to permit them to grow very large. Large ones produced in rabbits are shown in the chapter on Primary and Secondary Sex Organs.

In the previous section of this chapter we have referred to the role of dental infections in relation to the pancreas, and diabetes as seen in the clinical study of these cases. We have tried experimentally to produce typical diabetes by the inoculation into rabbits of cultures from the teeth of patients suffering from acute diabetes. The blood sugar of this patient was 130 mgs. per 100 cc. After the removal of her dental infections, she had a very sharp reaction which put her to bed for a few days. The culture grown from her tooth increased the blood sugar of the rabbit from 97 to 149 with a single injection of the strain. A reinoculation of the rabbit with this strain again produced a rise in the blood sugar. Figure 192 shows the normal histology of the pancreas of a rabbit. Figure 193 shows the pathological histology of the pancreas of a rabbit in which an artificial diabetes has been produced. A pathological pancreas has a decreased number of functioning Islets of Langerhans, which is a very difficult condition to reveal histologically.

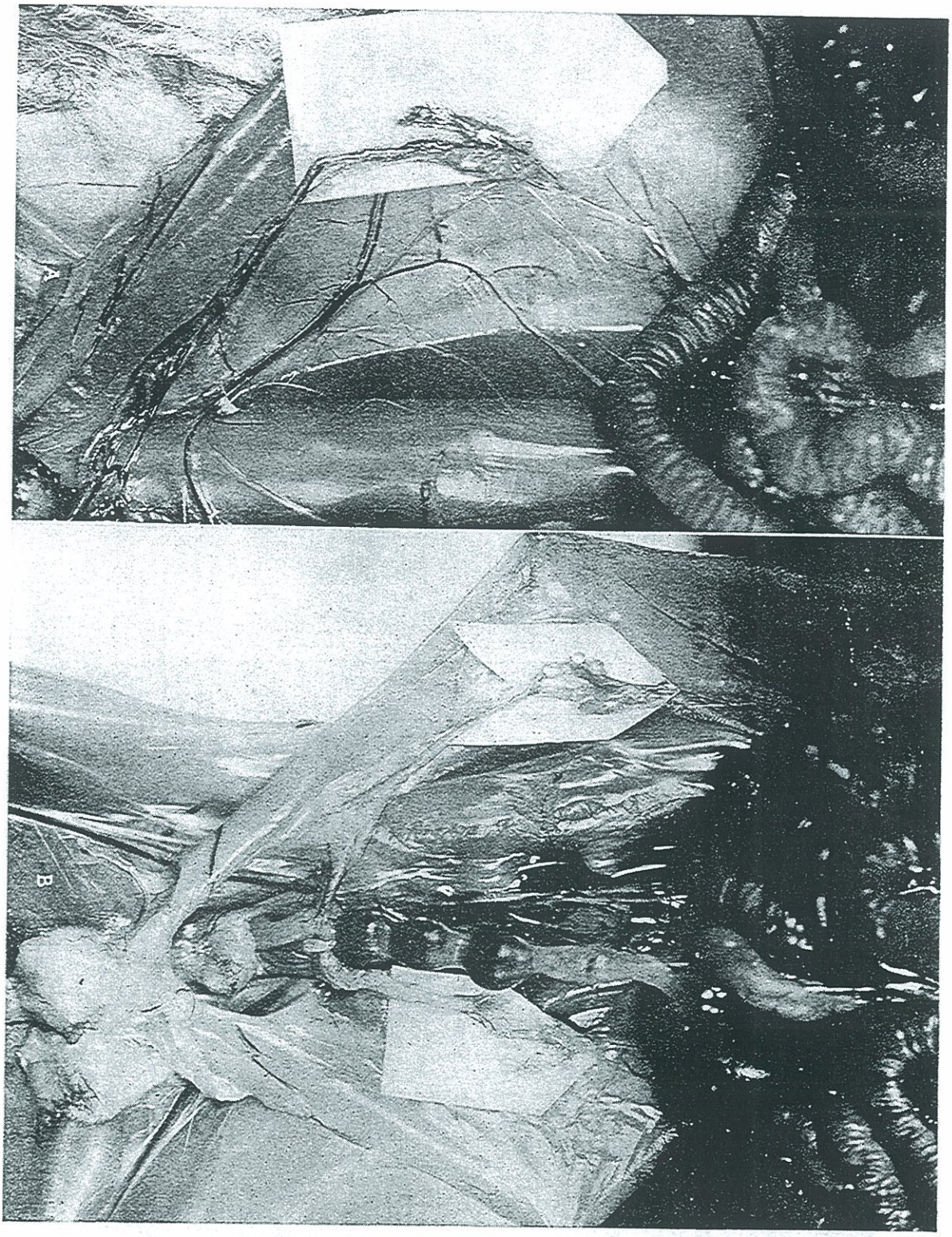


FIGURE 191. TWO RABBITS WHICH DEVELOPED OVARIAN CYSTS. PATIENT FURNISHING CULTURE HAD RECENTLY BEEN OPERATED FOR SAME.

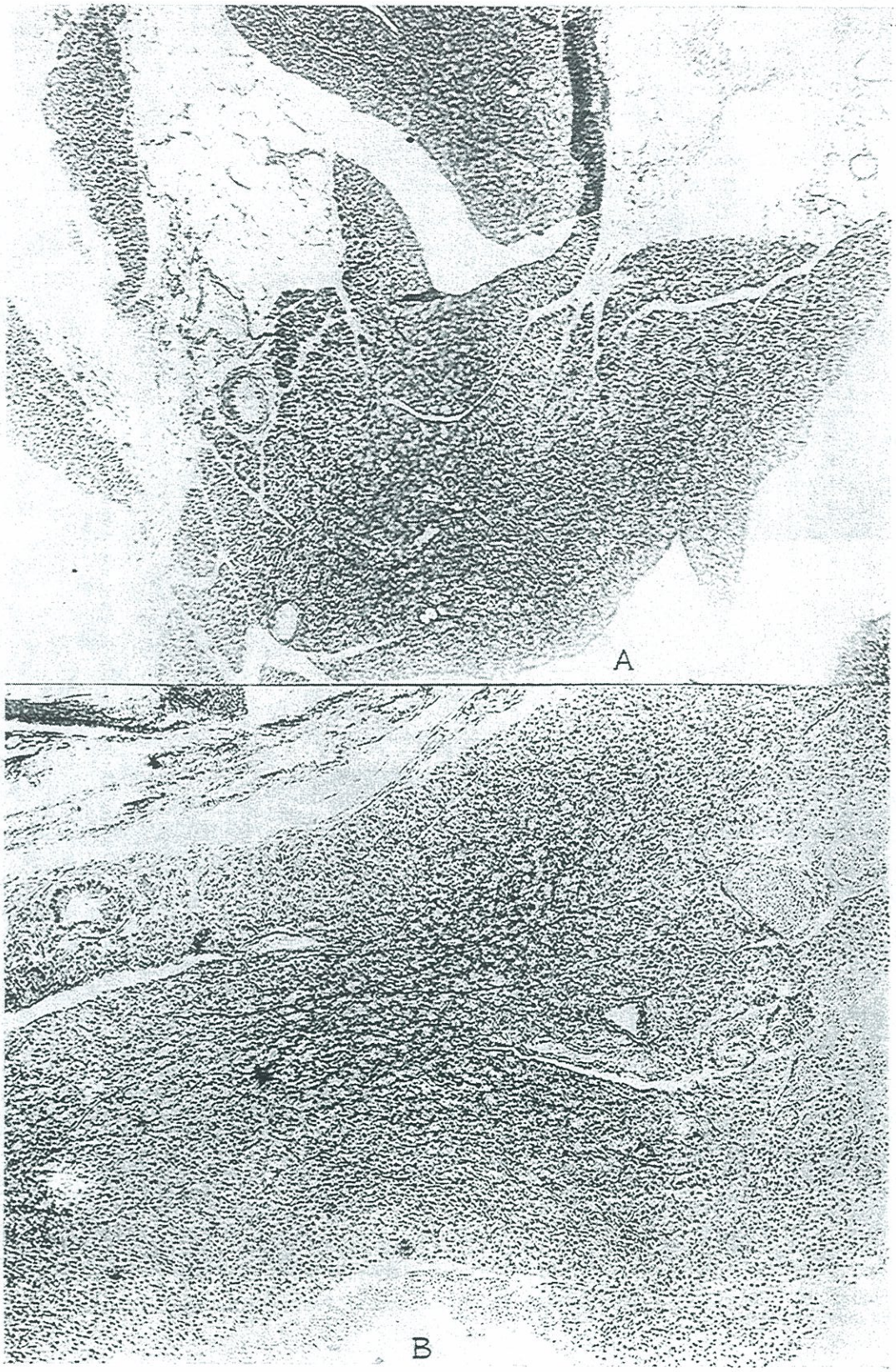


FIGURE 192. (A) NORMAL RABBIT PANCREAS.

FIGURE 193. (B) PATHOLOGICAL RABBIT PANCREAS.

The only interpretation we are able to make of these phenomena is that dental infections tend under certain conditions to involve the glands of internal secretions in the animals inoculated when these cultures are taken from patients suffering from acute involvements of these tissues.

III. THE MODIFICATION OF THE PATIENTS' SYSTEMIC INVOLVEMENTS PRODUCED BY DENTAL INFECTIONS BY THE ADMINISTRATION OF EXTRACTS OF THESE GLANDS.

One of our most difficult problems has been to ascertain the role of the glands of internal secretion in the presence or absence of a defense against dental infections. Relatively little is known as to what constitutes the chief elements in the mechanisms of defense. Some elements, however, seem pretty definitely established or at least strongly suggested. Since patients with a good defense have, as a group, a high ionic calcium of the blood in contrast with a relatively lower ionic calcium of the blood in patients with a low or broken defense, we seem justified in concluding that in some way this element, whatever the factors are which it may represent, is indicative of the nature of the defensive mechanism of the patient. In the preceding chapters I have brought out the following important facts:

With the elimination of dental infections there tends to be a marked rise in the ionic calcium of the blood, when it is depressed, with a reduction of the pathologically combined calcium of the blood, if we are correct in our interpretation of our data. In some cases, in spite of the elimination of dental infection, the patients remain on a low level, as though they fail to have the mechanism functioning which should bring about the reëstablishment of a normal defense and normal functioning. These cases are very slow to recover. In their case the prognosis is bad. They tend continually to recurrence and tend, in general, to have an unfavorable prognosis. We have endeavored to whip up the defense in these cases by various means such as autogenous vaccines and with very definite betterment in many instances. In some cases, however, in spite of the removal of the dental infections and the effort to whip up the defense with a vaccine, the results, as judged by the clinical improvement, have been very limited. This failure to improve physically has been paralleled by a failure of the ionic calcium to be improved toward normal. This has strongly suggested the absence of some activating substance which either

combines with the toxic substance of the involved infections, or which reinforces the patient's defensive mechanism.

In the chapter on Serological Studies we have showed the suggested relationship of the ionic calcium to the activity or normal functioning of the cells of the body. With an increase of the calcium beyond the normal, sugar readily passes from the blood, through the kidney, with the urine. We have tried the injection of ionic calcium in both rabbits and patients in such diminutions and quantities, as would make the absorption of the calcium readily possible, with limited success, as indicated by the raising of the ionic calcium of the blood. In some cases there would be a prompt improvement, which advantage would be lost, also, quite promptly.

In thyroidectomized dogs it was early found that there was a tendency to development of tetany. It was later shown, however, that this was due not to the removal of the thyroid but the removal of the parathyroids, for the animals from which the thyroid was removed, without the removal of the parathyroid, could be kept alive by the administration of thyroid extract, but would die if the thyroid extract were not administered; and, similarly, the removal of the parathyroids, without the removal of the thyroid, produced a tetany and death which, however, could be prevented by the planting in the animals' tissues of parathyroid tissue. In either case the animals lived if a small quantity of both thyroid and parathyroid tissue was left. It was also shown that the removal of the parathyroids was accompanied by a depression of the ionic calcium of the blood, and that the injection of ionic calcium into the blood stream of an animal developing this tetany, relieved the symptoms. This has strongly suggested that the parathyroids are very directly related to the metabolism of calcium.

I have, accordingly, endeavored to raise the ionic calcium of the blood by the administration of parathyroid extract to patients suffering from dental infections, from which they did not readily recover, after the removal of the dental foci. Such a case is the following:

Case No. 1267.—A man, fifty-seven years of age, presented with the following history. His mouth was closed by swelling, which developed some months after the extraction of a mandibular molar tooth of the same side, some months previously. This operation had been made under gas, which excluded the possibil-

ity of the local anaesthetic's having lowered the defense, locally, of the tissue, or of infection having been carried in with the hypodermic needle. It was exceedingly difficult to make a physical examination, due to the muscle spasm and the patient's prostration. He was so physically weak, that he had to be helped and almost carried into the ward. Pus was located and drained from the internal border of the ramus distal to the position from which the tooth had been removed, and no infection had developed through the socket which had healed. This man had other dental infections which were removed, and the sockets healed slowly, but completely. There was a continual recurrence of the disturbance of the tissues about the left angle of the mandible, with a final cellulitis and lymph adenitis. Two enlarged lymph glands were opened surgically by his surgeon; by the maintenance of packs in these incisions, drainage was maintained, which wounds, if permitted to close, caused him immediate return of more acute symptoms. This involvement of his neck seemed quite distinctly separated from any possible zone of necrosis of the mandible.

The ionic calcium of his blood, which would normally be about 10 to 10.5 mgs. per 100 cc., stood at 7.5; and the use of tonics and the removal of dental infections failed to bring it up appreciably, suggesting an unfavorable termination, as the case was progressively getting worse. The clinical picture was complicated by a history of previous positive Wassermans. Parathyroid extract, one-tenth of a grain per day, was administered by me to determine its effect in increasing the ionic calcium of the blood, as well as upon his general clinical condition. In addition to the administration of the parathyroid I placed him on a diet, intended to increase, as rapidly as possible, his ionic calcium: namely, two quarts of milk a day, or preferably the same quantity of buttermilk, and two or four tablets of calcium lactate with each meal. Promptly the ionic calcium of the blood began to rise, increasing about 1 mg. per month per 100 cc.; and with this improvement in ionic calcium, his physical condition improved; the flowing fistulæ in his neck and extensive induration subsided and completely disappeared; his general physical condition returned rapidly to normal, so that in five weeks' time he gained six pounds in weight, which was more improvement than is indicated by the weight, since a part of his previous weight was edema. He was able to take up his work in a few weeks' time, increasing his hours rapidly,

and in approximately eight weeks was carrying his original heavy load with several extras; and in twelve weeks, according to one of his associates, was doing much more than an ordinary man's capacity of the hardest kind of mental and physical work.

EFFECT OF PARATHYROID AND CALCIUM LACTATE TREATMENT ON IONIC CALCIUM OF BLOOD

Date	Hour A. M.	Treatment for Ionic Calcium	Ionic Normal Serum	Ionic Treated Serum	Combined Patho-logical
8–31–22	9:00	Began	7.5	9.7	2.2
9– 6–22	10:00	Continued	7.9	9.9	1.9
9–13–22	11:00	Continued	8.1	9.5	1.4
9–26–22	11:00	Continued	8.2	9.4	1.2
1–24–23	11:00	Discontinued	10.6	11.0	0.1
2–16–23		Resumed	9.2	11.1	1.8
4–25–23		Continued	9.4	9.9	0.5

FIGURE 194.

The progressive changes in this case are shown in the table in Figure 194.

Another striking case is as follows: A young mother, who had had a miscarriage soon after the birth of her previous child, was suffering from rheumatism, probably related to dental infection. The ionic calcium of her blood was 8.2. In two weeks' time after the removal of her dental infection and with the assistance of parathyroid and calcium lactate, her ionic calcium had increased to 10.4, her rheumatism had disappeared, and instead of being discouraged and despondent, she had regained her normal state of vivacity, hopefulness, and pleasure in life.

But all cases do not respond thus readily to the administration of parathyroid. In contrast with the above, I will cite the following: This patient had multiple deforming arthritis. His ionic calcium was reduced to 7 milligrams, with 3 milligrams pathologically combined. He was placed on a special diet of milk, calcium lactate, and a general mixed ration plus parathyroid. His condition improved but slightly, though definitely, but tended rapidly to settle back to his former condition. Removal of his dental infections did not materially improve his general condition which had existed for several years. The administration of parathyroid and calcium lactate only increased his ionic calcium from 1½ to 2 milligrams. There was evidence that he was suffering from some other source of toxic involvement, that was so extensive, as to

keep him continually overwhelmed. He was referred to specialists for the study of his digestive tract; and after being placed on a rigid rest treatment combined with hydrotherapy, he became more comfortable but with only slight improvement. They found a chronic colitis, which it seemed probable accounted for these symptoms and general reactions. The patient had felt definite improvement from the milk diet and requested that he be placed on that exclusively, of which he took four quarts daily. The result was that he experienced a marked improvement in the arthritic disturbances, and his ionic calcium coincidentally increased about four milligrams. We interpret these results as follows:

On the milk diet, there was a distinct change produced in the bacterial flora of the entire intestinal tract, particularly of the colon, coincidentally, a change in the acid-base balance of the fluids of that tract. The toxic substances to which he had become sensitized and which were produced in that tract were reduced because of the reduction of the flora that had generated them. With the elimination of this toxic source, his blood was able to maintain its ionic calcium which otherwise was neutralized by this toxic substance, besides which there was undoubtedly a distinct beneficial effect upon this local tissue from the presence of the milk products. The increased ionic calcium of the blood would rapidly raise the defense and repairing power of the diseased tissues of the colon; and just as the vicious cycle had tended to get worse and worse previously, similarly, by the increase in ionic calcium of his blood, the repairing power of the local tissue increased and the absorption of toxins decreased, the significance of which seems to be, that the administration of parathyroid and the forced intake of a calcium furnishing diet will be of no avail in a system suffering severely from the presence of a toxic generation and absorption of the same or similar type as that in a dental focus with which we are concerned; and this explains probably in large part why the removal of the dental infection produces in many cases either a temporary or a limited beneficial effect.

IV. THE IMPROVEMENT OF THE FUNCTIONING OF THE GLANDS OF INTERNAL SECRETION BY THE MECHANICAL STIMULATION INDUCED BY THE MOVEMENT OF THE BONES OF THE FACE AND BASE OF THE SKULL.

One of my earliest experiences, in this connection, was with a case which showed conspicuously the interrelationship between

the pituitary and the development of the bones of the face. This boy at the age of sixteen was infantile in many of his characteristics and developments. The genitals were those of a boy eight years old. The facial expression was that of the typical Mongolian idiot. By the Binet test he had a mentality of about four years. Roentgenograms of his hands showed that the epiphyseal bones had not united. He played on the floor with blocks and with rattles like a child. His interest was in children's activities.

The characteristic physical condition was that his maxillary arch was so much smaller than the mandibular arch that it went entirely inside it. In order to give him a masticating surface and with the hope of helping him both physically and mentally, since I had had several cases greatly benefited by such an operation, I determined to widen his arch by moving the maxillary bones apart about one-half inch. The position of his teeth before is shown in Figure 195-D. Roentgenograms showing the opening of the median suture with increase of pressure are shown in Figure 196.

An important phase of this case was that the left nostril was entirely occluded and had been probably all his life. A rhinologist spent a half hour trying to shrink the tissue with adrenalin and cocain sufficiently to get air or water through, and was not able to do so. He was able to breath only through his mouth. The quantity of air that he was able to secure through his right nostril was so scant that he continually breathed with his mouth open. At night he was forced to lie with something like his coat rolled into a ball and placed under the back of his head and his head pushed far back so that this position would open his mouth and retain it so, or he would awaken by strangling himself with the closing of his mouth.

He had the innocence and utter lack of sense of modesty of a child; would undress under any conditions before strangers. With the movement of the maxillary bones laterally, as shown progressively in Figure 196, there was a very great change in his physical development and mentality. He grew three inches in about four months. His moustache immediately started to grow; and in twelve weeks' time the genitals developed from those of a child to those of a man. His mentality change was even more marked, as the median space between the maxillary bones was widened to one-half inch in about thirty days, and by some process which I have interpreted as probably being a prying down of the base of the skull, thereby reducing by the leverage of the

FIGURE 195. FRONT VIEW. CHANGES PRODUCED BY SLOWLY OPENING THE MEDIAN SUTURE. CASE NO. 111. AGE SIXTEEN. IN ABOUT TWELVE WEEKS HE PASSED THROUGH THE CHANGES OF ADOLESCENCE, RAPIDLY GROWING A MUSTACHE, ETC.

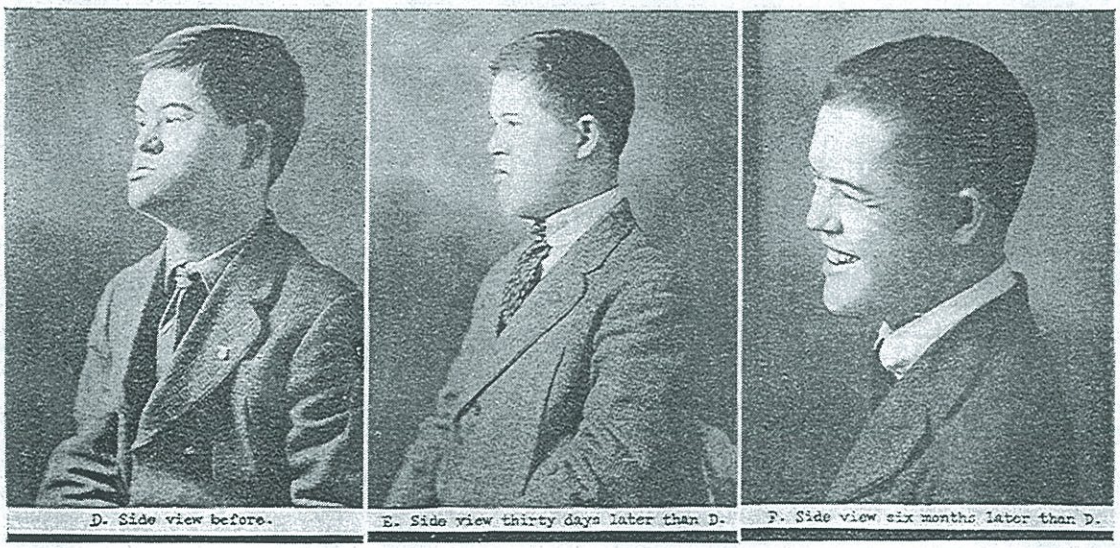


FIGURE 195. SIDE VIEW. CHANGES PRODUCED BY SLOWLY OPENING THE MEDIAN SUTURE. CASE NO. 111. AGE SIXTEEN. THE MENTAL CHANGES WERE ALSO VERY GREAT. HE PASSED FROM PLAYING WITH BLOCKS TO THE INTERESTS OF DEVELOPING BOYHOOD, TELEPHONING, READING, ETC.

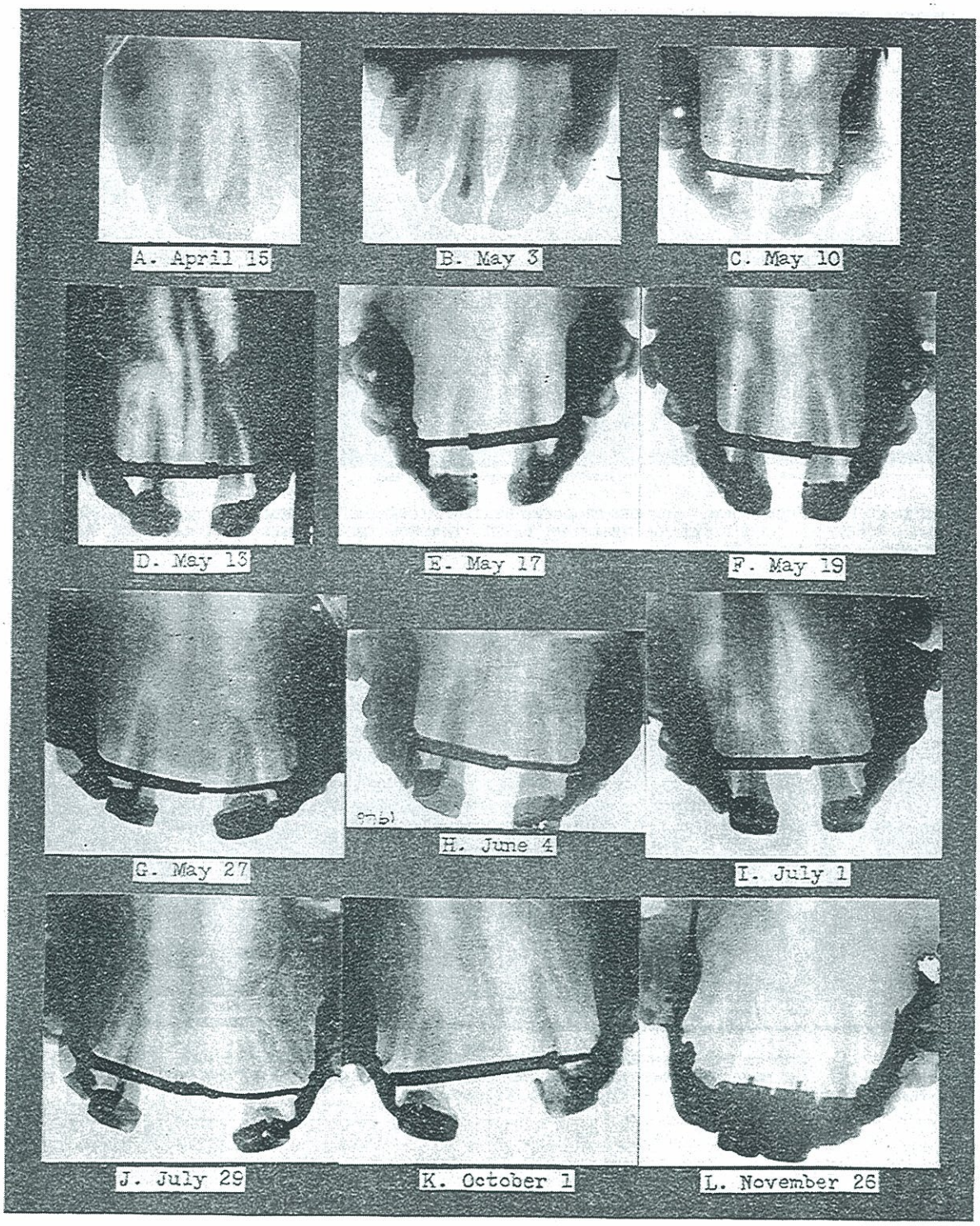


FIGURE 196. ROENTGENOGRAPHIC CHANGES BY DAYS FROM OPENING THE MEDIAN SUTURE.

maxillary bones on the temporal bones, a pressure upon the hypophysis cerebri or pituitary in the sella turcica, and thereby markedly changing its function. In a few weeks' time he passed through stages that usually take several years; at first, getting behind the door to frighten us, later, putting bent pins on chairs to see us jump when we would sit down, and finally being the cause of a policeman's coming into the office from where he was conducting traffic on the corner below to find who it was squirting water on him when his back was turned. He developed a great fondness for calling people over the telephone, wanted to borrow my automobile to take his mother for a drive, and with his arm caressingly about the shoulders of one of the secretaries invited her to go with him to Euclid Beach for a dance. All this change developed in about twelve weeks' time.

A most remarkable event happened in connection with this procedure. He lived in another city, and so, while with me was kept in a boarding house at a little distance from my office in order for frequent and necessarily constant attention. On his return to his home town with the appliance to maintain the separation in place, his efficiency had increased to such an extent that his mother would send him with the money to the grocery store with the order for the day's groceries, and he could invariably bring back the right change and could tell when it was correct. He could also come to me that ninety miles by railroad and make two changes of trains and the various transfers on the street cars of the city with all the exactness of a normal adult.

But this appliance became dislodged; the maxillary bones settled together; immediately, or in a day or two, he lapsed into his old condition of lethargy accompanied by an old trouble, which had frequently been distressing, of nausea, sometimes lasting for twenty-four hours. With the readaptation of the separating appliance and the reconstruction of the retaining appliance he returned again to his other state.

But a new problem had been developed. We had changed an infant to a potential man with all of the instincts and impulses of a man but with the mind of a child. It became necessary for his family to make changes because of the death of his mother, and the marriage of his sister, and he was accordingly placed in a state institution where he was lost in the herd, all receiving approximately the same care. During this period under which he was in my care he had learned to read and spent much time doing so.

Figure 195 shows his appearance before and after the operation, there being only thirty days' difference between each A and B, and D and E, side view. C and F show, respectively, the front and side views six months after the first picture, and it will be noted that his whiskers and moustache had started to grow. He now has the face and potentialities of a man.

In this connection I would refer to another case where a boy of eight years had less marked depression of the maxillary arch but a very marked depression mentally, such that he was not able to be taught with other children. An important characteristic of his case was that he was as timid as a bird and as dependent as an infant, was afraid of all children who might in any way cross him for fear they might hurt him, and was extremely docile to his parents. After the separation of the maxillary bones, similarly, though not so extensively, as in the latter case, his condition improved so greatly that his mother could send him to the store with the money to buy provisions and groceries and he could return with five articles which he would buy himself, and not forgetting even one. He also became the bully of the street; would come into his home boasting about how he had smashed such a big boy's nose for crossing him in something; and finally when his mother chided him for something that he did not wish to do, stating that she could not have anyone in her home who did not mind, he promptly told her that if she insisted on his doing that thing that he would leave the home. This was a complete change from his former lack of assertiveness and capacity for individual defense and responsibility. Unfortunately, domestic conditions made it necessary for this boy to be moved away from this city and for three years he was out of my care and received no attention. The final results were not so good as they should have been because of this neglect, though he never lost his assertiveness and capacity for taking responsibility.

SUMMARY AND CONCLUSIONS.

We would summarize these studies as follows:

(1) Disfunctions of various of the glands of internal secretion are often very materially corrected, and sometimes completely so, by the removal of dental focal infections.

(2) Involvements have frequently been produced

in similar endocrine tissues of the animals by inoculating them with the cultures from the teeth of the involved patients.

(3) The administration of the extracts of the glands of internal secretion, particularly of the parathyroid, is shown to be of distinct benefit in certain cases of depressed ionic calcium of the blood, due in part to dental focal infections, where this improvement has been absent or slow following the removal of the dental infections.

(4) An improvement has been produced in individuals, which we interpret to be due to a stimulation of the pituitary body, which in turn doubtless stimulates other ductless glands and together with them produces a marked change in both physical and mental states.

See bibliography references 20, 21, 22, 23, and 24.

CHAPTER XXXVIII.

THE NATURE AND FUNCTION OF THE DENTAL GRANULOMA.

PROBLEM: Is a dental granuloma a pus sac and its size a measure of the infection and danger?

EXPERIMENTAL AND DISCUSSION.

It is not without significance that the members of the laity speak of the structure which is frequently attached to an extracted root as a pus sac and something greatly to be feared and dreaded. They have very correctly reflected the thought of the professions. These researches have been undertaken to harmonize, if possible, the data that have been developed in the preceding researches here reported and the current opinion. If we were to express the public and professional evaluation of this structure it would be as follows:

Since a dental infection, if present, will produce an apical abscess, the size of that abscess will be the measure of that infection; and if it be particularly bad, it will produce a pus bag or sac which may or may not contain pus, but which is always an evidence of considerable infection.

In Chapter 3 on The Local Structural Changes Produced by Dental Infections, we found (1) that there is a large variation in the periapical structural changes that will be produced with an apparently given quant ty of infected pulpal irritant, sufficient that these individuals may be graded from those having large apical involvements associated with, for example, a putrescent pulp; (2) those with this large area of apical involvement but which, instead of being diffused into the cancellous structure, is surrounded by a more or less definite zone of condensed structure, a condensing osteitis surrounds the zone of rarefying osteitis; (3) a very limited zone of destruction of apical bone with frequently a tendency to a dense bone surrounding the apical area.

In Chapter 4 we found that there is a very great difference in the susceptibility of individuals to injuries from dental infections expressing themselves as rheumatic group lesions.

In Chapter 5 we found that the individuals with the high de-

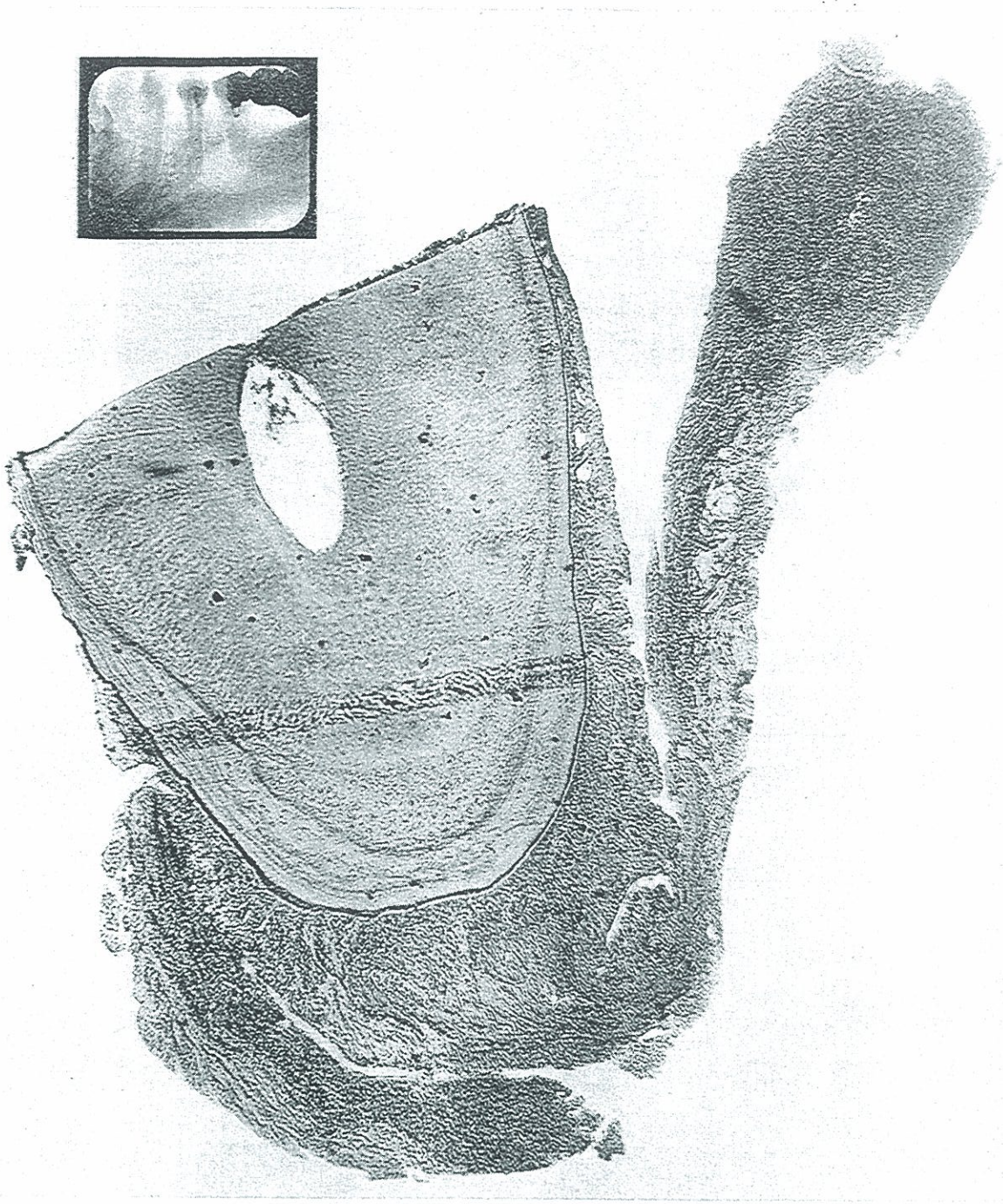


FIGURE 197. APPEARANCE OF A DEGENERATING GRANULOMA. PATIENT HAS LOST HER DEFENSE. INSERT SHOWS ROENTGENOGRAPHIC APPEARANCE.

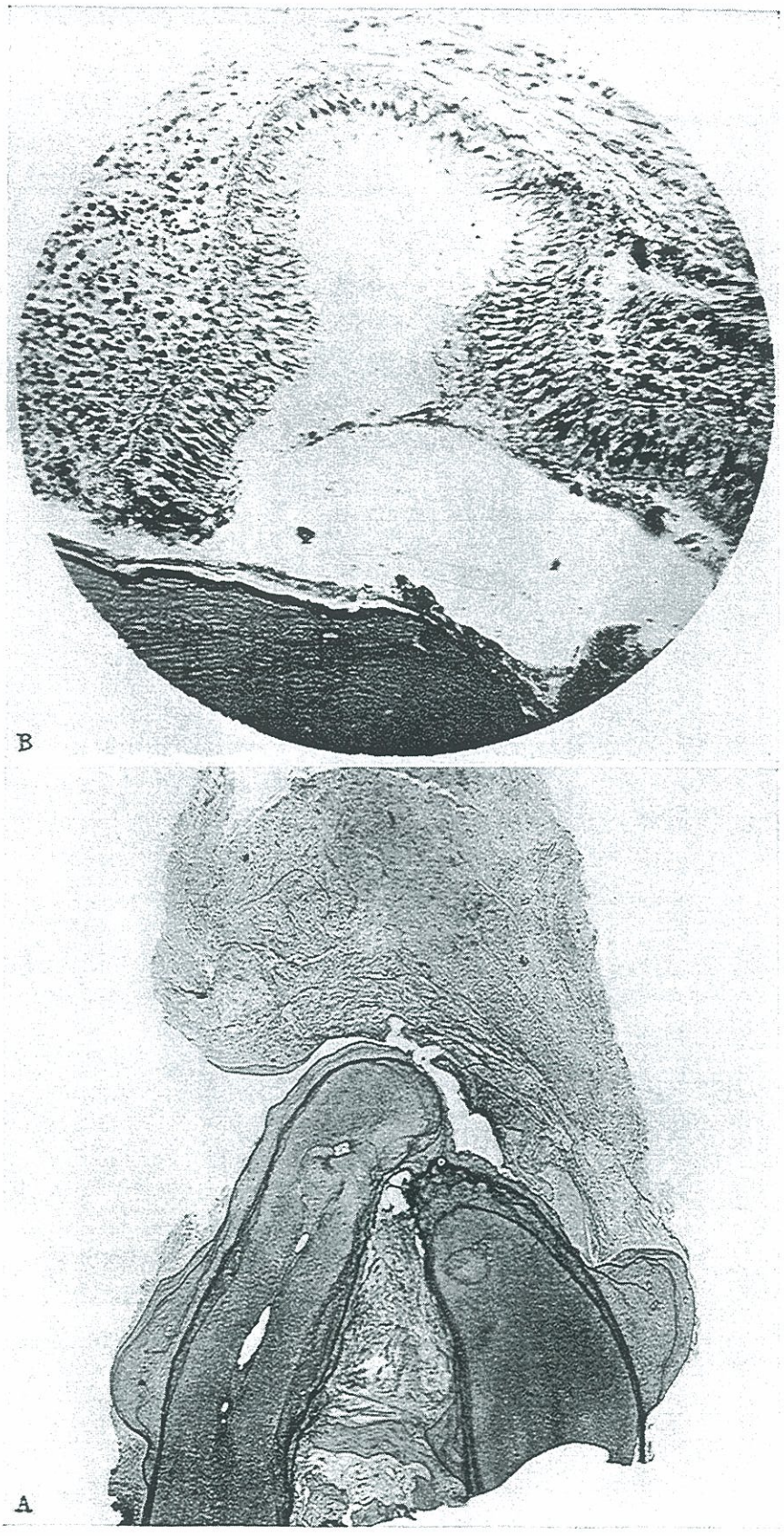


FIGURE 198. A PROTECTIVE MECHANISM OF DENTAL GRANULOMATA.

fense which protected them against injury from their dental infections (expressing themselves systemically as rheumatic group lesions) had invariably a relatively larger zone of rarefaction or bone destruction about the apex of an infected root, than did the individuals without that defense, in whom the dental infections expressed themselves readily as rheumatic group lesions; and that the individuals showing the zone of condensing osteitis surrounding the zone of rarefying osteitis generally proved to be individuals whose defense had previously been high and had been reduced, which latter we termed a state of an acquired susceptibility. This latter classification was based not on this local structural condition, but on the fact that the patient, that had previously had complete freedom from rheumatic group lesions, had suddenly acquired that condition, hence an acquired susceptibility.

Subsequent chapters revealed that dental caries tended to be much more dominant in the individuals with rheumatic susceptibility, and periodontoclasia tended to be more prominent in the individuals without the susceptibility to rheumatic group lesions.

In the chapters on serological and chemical changes in the blood and fluids of the body, the data revealed that in the individuals with a high defense, the ionic calcium of the blood tended to be high; and that it tended to be lower than normal in those with a rheumatic susceptibility; and that in the same individual, generally just in proportion as the ionic calcium returned to normal, the rheumatic group symptoms disappeared; also that these variations were produced regularly in animals by the introduction of dental infections either by inoculations or by the planting of the infected tooth beneath the skin.

These studies, and the data they revealed, strongly suggested that the tissue which developed at the root apex, and which was present in relatively larger quantities in those individuals with a high defense, was a defensive tissue placed there by Nature to establish and maintain a quarantine as close as possible to the source of infection. I, accordingly, have made a very careful study to ascertain the nature of the tissue producing this quarantine and have found a very large range in the types of tissue found at root apices. Figure 197 shows a granuloma removed with the tooth of a patient who up to six months ago had a very high defense and no rheumatic group symptoms, but during the past six months following a cold or Flu she has had quite persistent neu-

FIGURE 199. HIGHLY VASCULAR GRANULOMA OF FIGURE 198.

ritis. Note the very large lumen in this granuloma, consisting of necrotic tissue, leucocytes, and bacteria. The insert shows the roentgenogram of the tooth before extraction, and it will be noted that there is a definite zone of condensing osteitis surrounding the area of rarefaction.

In Figures 198 and 199 we see in contrast with this a granuloma which is intact, very highly vascular (shown in high power in Figure 198-B) with no necrotic and degenerated tissue, and with a very distinct epithelial membrane in contact with the root apex. These two quite divergent pathological structures are but two of a very wide range which might be inserted; and they and the structure represented in Figure 200 are presented here simply to suggest the extreme variation that may occur in these apical tissues.

In Figure 200 we see a very limited amount of fibrous capsule lying close to the denuded root end, almost entirely without vascularization, with a purulent exudate between the membrane and the tooth. I will later discuss and interpret these conditions.

If the dental granuloma is simply Nature's method of encysting a foreign substance or an irritant, it must be considered a quite different structure from that which Nature will build into a zone as the result of irritation, in which case the irritation would produce a proliferation and hence, as its name implies, a granuloma, for this is, we take it, the origin of the name that this tissue has taken. For example, Dorland's definition of a granuloma is as follows: "A tumor or neoplasm made up of granulation tissue. Dental g., a small mass of granulation tissue containing bacterial depcsits on the root of a tooth." Anthony's is: "A tumor-like nodule or area of granulation tissue. Dental g., granulation tissue about the apex of a tooth usually containing bacterial deposits. Chronic inflammatory pericementitis." Ottofy's is: "A collection of leucocytes and epitheliod cells which surround the central point of irritation and resemble granulation tissue. Dental g., granulation tissue, without suppuration, at the apex of the root of a tooth or in some edentulous tissues."

Our first line of approach was to determine what Nature's reaction tends to be to mechanical irritants, in order that we might distinguish clearly between mechanical irritation and bacterial irritation. To determine this, I placed various foreign substances in the tissue under the skin of rabbits and found that if the object were sterile when inserted, Nature developed a very slight trans-

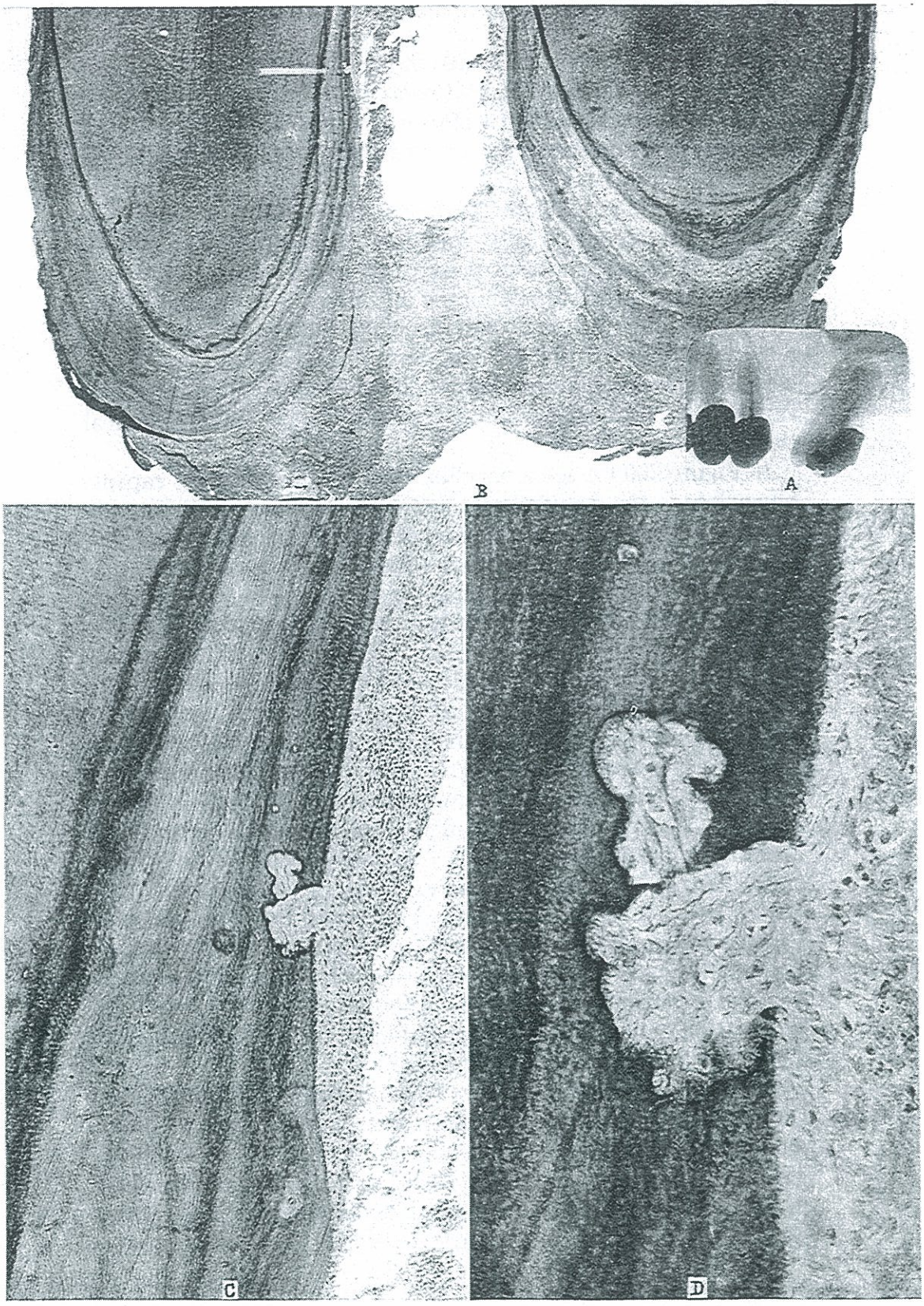


FIGURE 200. RESORPTION PROCESSES IN C AND D, FROM POINT OF ARROW IN B; A, ROENTGENOGRAPHIC APPEARANCE.

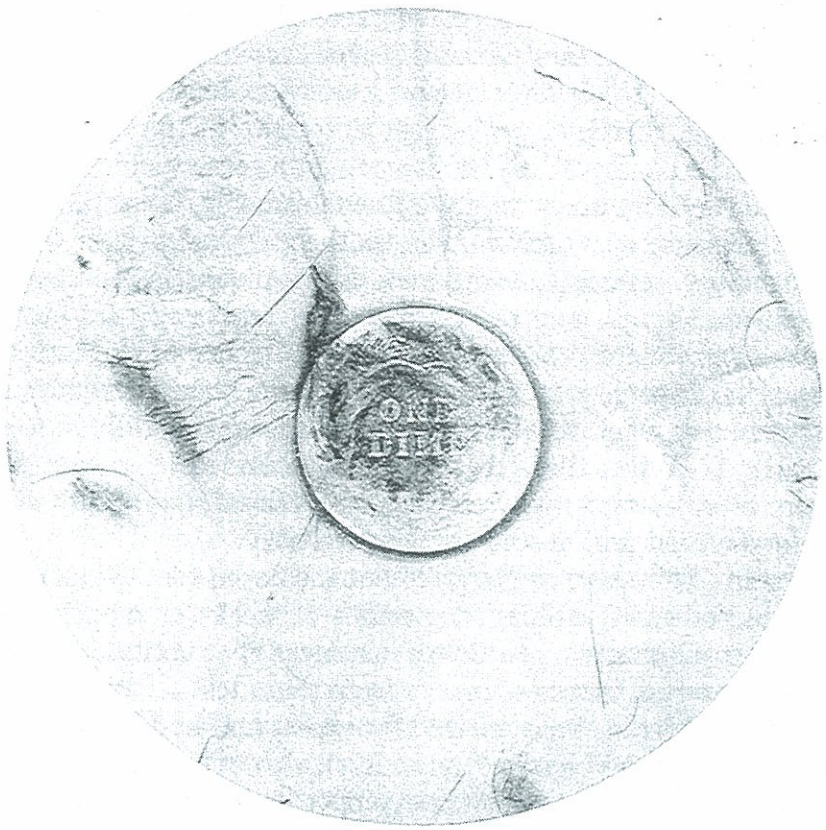


FIGURE 201. APPEARANCE OF DIME PLANTED TWO MONTHS. NOTE NO CYST FORMATION.

parent fibrous tissue about it with no tendency to proliferation or development of granulation tissue. This is well illustrated in Figure 201 which shows a dime so encysted in the tissue of a rabbit, it having been placed beneath the skin in this position two months previously. These have been left for longer and shorter periods, and the only change that is apparent is a definite evidence of etching and solution of the metal. It may be answered that this is due to the formation of albuminates with the silver and that the effect would be different with other metals. We have found little or no difference whether the foreign irritant was a piece of sterile glass or a piece of any one of the ordinary metals. It will be noted that the inscription on the dime, shown in Figure 201, can be read through the capsule as though there were no intervening tissue.

When we have placed teeth beneath the skins of rabbits or in other tissues such as the muscle, as we have now done over a hundred times in various studies, we find a very great difference in the effect. If the tooth has been free from infection, as, for

example, a freshly extracted impacted third molar, there is very little more tissue built around it than around the dime shown in Figure 201. If, however, it was a pulpless tooth, with or without root filling, there is a very great difference in the reaction which it produced, ranging all the way from a closely adherent fibrous capsule entirely surrounding and enclosing the tooth, to the complete absence of a capsule, the tooth being found in a well of inflammatory exudate, sometimes with a quantity of leucocytes dead and living, and sometimes with practically no leucocytes and a pure culture of streptococci. In either of the latter cases when no capsule was formed, the rabbits were invariably killed in from a day and a half to a few weeks; and generally in less than six days. When these teeth were surrounded by a capsule they were often carried many months or a year if the rabbits were not chloroformed and posted earlier for study.

Figure 202 shows a group of encapsulated teeth that had been in the bodies of rabbits for periods of weeks or months, several of them six months. In many instances the rabbits did not show the slightest evidence of injury from these teeth. In some others, even though they were carried for weeks and had become entirely encapsulated and showed no evidence to develop local abscesses about the teeth, the rabbits developed degenerative diseases such as involvements of the heart and kidneys. Figure 203-A shows a rabbit with such a tooth placed beneath the skin, which had been taken from the mouth of a patient with nephritis. The rabbit developed acute nephritis, as evidenced by albumin in the urine, development of casts, and parenchymatous degeneration of the kidneys, as shown in B and C. In Part Two, other volume, in the study of the relation of dental infections to the degenerative diseases, I show in Chapter 63 on Nephritis a case where the same tooth placed under the skin of two different rabbits developed nephritis in two rabbits in succession, where the tooth had been taken from a patient suffering from acute nephritis.

Invariably when the rabbit built a capsule about the tooth, it proceeded to absorb the tooth; and the process is not distinguishable histologically from that process when it takes place in the mouth. Figure 204 shows a cross section of one of these fibrous capsules developed by the rabbit in comparison with the structure built about a tooth by the human; and it will be noted that, histologically, it is practically impossible to distinguish which tissue was taken from the rabbit and which from the individual. It does

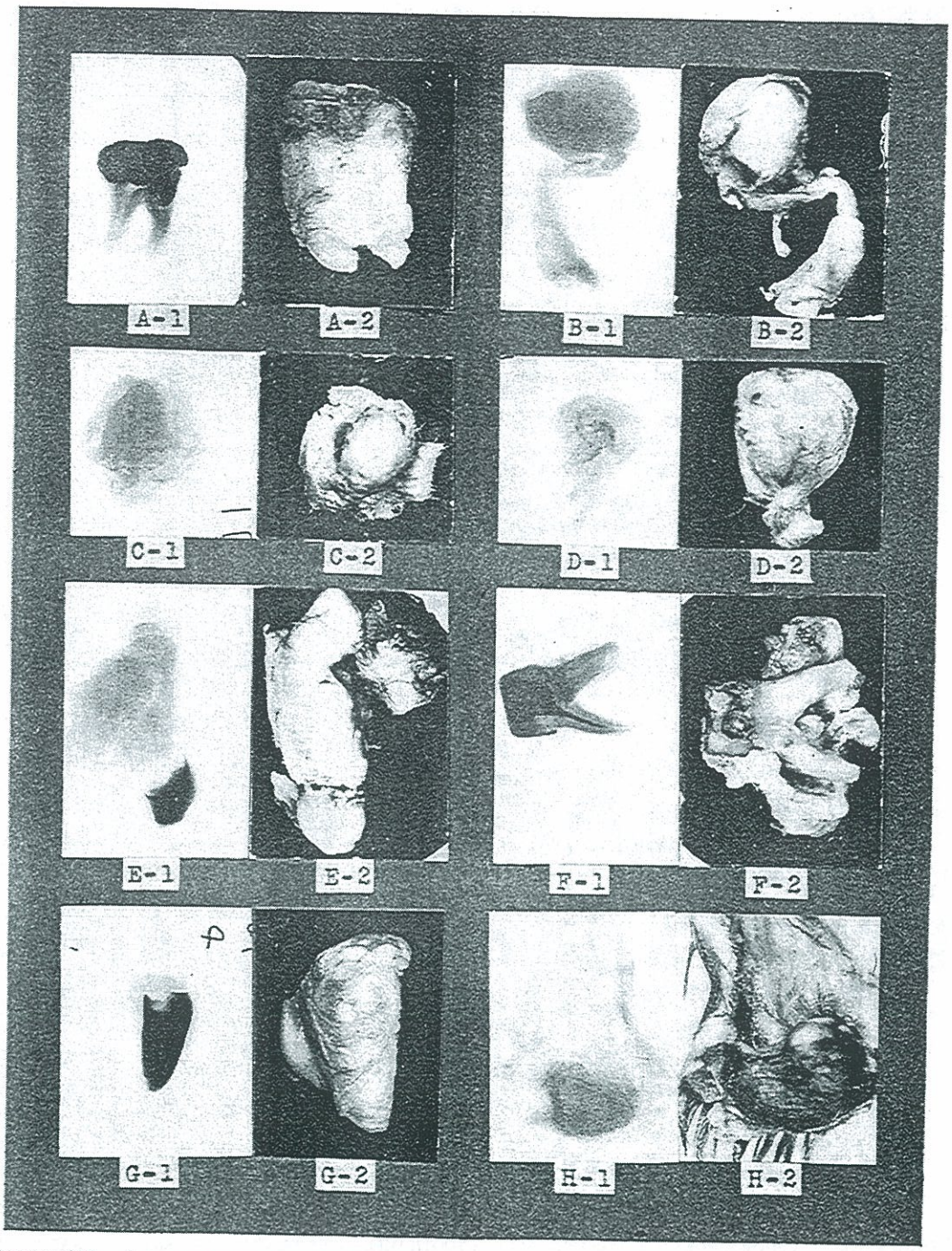


FIGURE 202. A GROUP OF ENCAPSULATIONS ABOUT IMPLANTED TEETH, PRODUCED BY THE RABBITS, AND THE ROENTGENOGRAPHIC VIEWS OF SAME. NOTE ABSORPTION OF TOOTH, B-1, C-1, D-1.

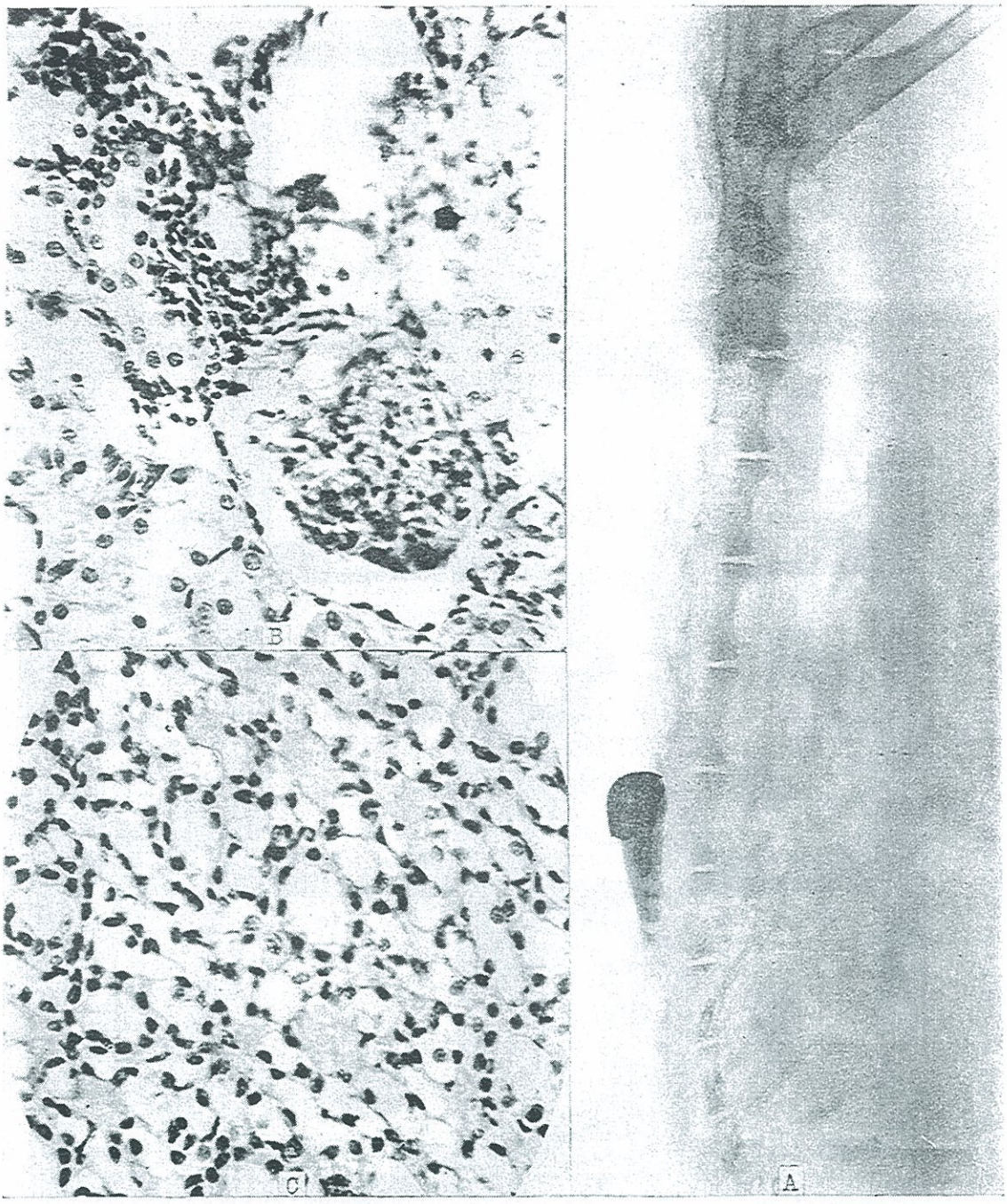


FIGURE 203. A SHOWS, ROENTGENOGRAPHICALLY, A TOOTH IMPLANTED BENEATH THE SKIN OF A RABBIT, WHICH HAD BEEN REMOVED FROM A PATIENT SUFFERING FROM NEPHRITIS. B AND C SHOWS TWO SECTIONS OF THAT RABBIT'S NEPHRITIC KIDNEY WHEN IT WAS CHLOROFORMED SOME WEEKS LATER.

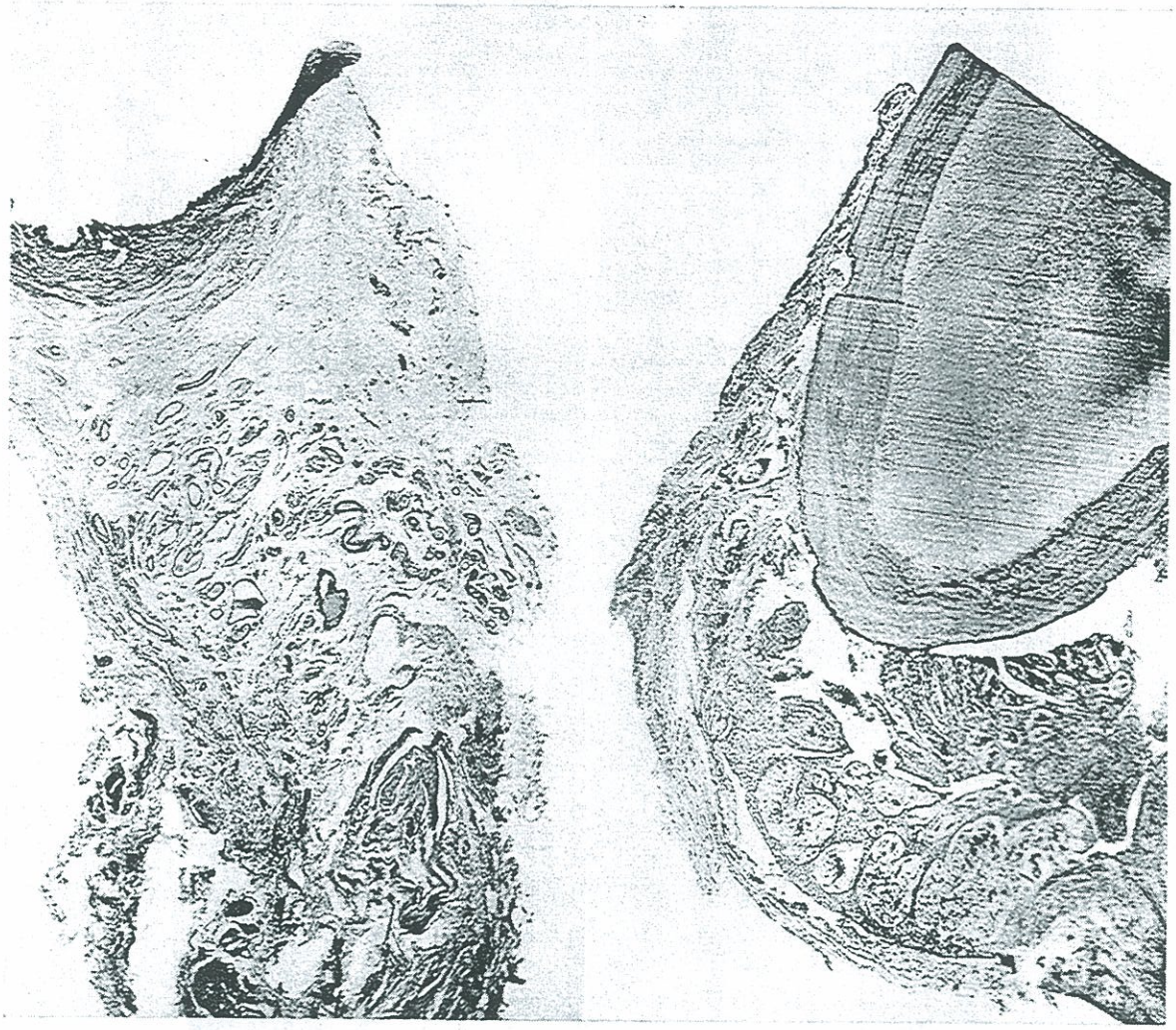


FIGURE 204. TWO GRANULOMATA. THE LEFT WAS DEVELOPED BY THE RABBIT ABOUT THE IMPLANTED TOOTH; THE RIGHT BY THE PATIENT FROM WHOM THE TOOTH WAS EXTRACTED.

not seem justifiable to think of the protective tissue built by the rabbit as a neoplasm; but, if so, why less justifiable so to think of the structure built about the same tooth by the patient from whom it was extracted. With regard to the histological picture presented by a tissue engaged in the process of absorption of the root of a tooth, it will be noted that it is also not possible to distinguish between the structures engaged in this operation, whether taken from the human or the rabbit.

If, then, all rabbits were affected systemically if they did not succeed in building a protective membrane about the tooth, while all survived apparently uninjured if they succeeded in doing so,

FIGURE 205. SHOWS AN ABSCESS PRODUCED UNDER THE SKIN OF A RABBIT BY THE IMPLANTATION OF A ROOT OF THE MOLAR SHOWN IN C. SEE TEXT.

we find to this extent a co-operation of our interpretations as made in preceding chapters. But this is not all the evidence herewith developed. It may be argued that while a tooth does not furnish either teacupfuls or quarts of organisms, there is still too great a quantity of infection for a rabbit to neutralize. If this be true, one rabbit should neutralize some part of the infection and toxin of a given tooth, and if that tooth should be transferred immediately to another healthy rabbit, we should expect that soon all of the poison in that tooth could be neutralized by the several rabbits. Assuming that an individual is twenty times as large as a rabbit, twenty rabbits might be expected to furnish enough neutralizing power to destroy this activity, whatever it may be in a given tooth. This has been tested incidentally in connection with another problem in which the same tooth was planted beneath the skin of thirty different rabbits, twenty not proving to be sufficient, and the last dying in as short a time as the first, and all but one within six days after the tooth was placed beneath the skin of the rabbit. One lived ten days and it was an exceedingly large and vigorous male who was so ugly a fighter that he tried to kill any other males that were put into the same cage. Within six hours after the tooth was planted beneath the skin, all this pugnacity and viciousness had disappeared, and in a couple of days the typical blood changes with loss of weight appeared.

In the chapter on calcium in relation to dental infections I have referred to the fact, that the ionic calcium of the blood of individuals affected with dental infections, is practically always depressed at the time that they are suffering from rheumatic group lesions; and, further, that if the patient's tooth be placed in the serum of that patient's blood, the ionic calcium is still further and very rapidly lowered, in some instances almost entirely removed from the serum. It can be regained by chemical procedure, as I have shown, for it is apparently in what I have termed a pathologically combined state with the toxin from the tooth. In these rabbits in which teeth have been planted beneath the skin, there has been a marked difference in the change of ionic calcium of the blood whether the animal succeeded in building an encapsulation about the tooth, in which case it generally lived for weeks or months, or whether it was unable to do so. In the former the ionic calcium remained practically constant and normal, while in the latter it was always reduced. With the reduction of the ionic calcium there was always a loss in weight of the animals

and the decline was practically in direct proportion to the depression of the ionic calcium, so much so that we could tell almost precisely when a rabbit would die by plotting the curve as the calcium was going down. This is shown in Figure 136 in the chapter on changes in blood calcium. I have stated, as was shown in very many cases in our rabbit posts, that invariably if the rabbit failed to build quickly an encysting membrane about the tooth, death followed promptly and practically always within ten days, in the majority of instances in five days or less, and often within two days. We can scarcely imagine a concentration of poison so profound that the small quantity that would be present in an ordinary root-filled tooth could overwhelm thirty rabbits in succession from a single tooth, and in which all the other teeth from that same patient produced the same effect. We are evidently dealing here with forces that are different from those that enter into our ordinary conception of cause and effect. In preceding chapters I have shown that by washing the crushed tooth and passing the washings through a Berkefeld filter and having a small quantity of apparently clear water left, I would have a substance which, when inoculated into the rabbits, would frequently start them on a decline, even though it was bacteria-free as proven by culture, and which decline would frequently terminate in death in a few weeks, and practically always with a depression of ionic calcium and of body weight.

In the chapter on the efficiency of root fillings (Figure 105) I have shown a case where a tooth, the second molar, was root-filled by us a year previously because we considered it a favorable condition to sterilize and root-fill. The roentgenograms of these teeth and one of the rabbits with the root implanted are shown in Figure 205. A shows the tooth before treatment and root filling, B immediately after root filling, and C seventeen months after root filling. The results of the root filling were quite satisfactory in accordance with the teachings available for the profession at this time. Roentgenographically the very slight zone of rarefaction at the apex of the root had grown less. But the patient was not as well as she should be, with symptoms which I suspected might be related to this tooth; and because of the great improvement she had had from other extractions, she desired to have it removed. This we did. The two roots of this molar were placed beneath the skins of rabbits. One root, the mesial, evidently contained much more toxic substance than the other for, as shown, the first rabbit died in six days. The subdermal abscess

is shown in Figure 205-D. The tooth was replanted in another rabbit which died in eleven days. Before it was replanted and after it had killed the first rabbit, I drilled into the apex at the foramen of the tooth after sterilizing the surface (these teeth are always thoroughly cleansed externally before being transferred to another animal) and cultured the borings and found that they contained a pure strain of streptococci, notwithstanding the splendid appearance of the root filling. The rabbit in which the other root, the distal, was implanted was able to encapsulate it. It died in twenty-three days. This root was then transferred to a second rabbit and it in turn encapsulated the root and died in thirty-seven days.

It should be noted that the second rabbit in each of these cases lived much longer than the first, which has a direct bearing on a criticism of this work, which I refer to elsewhere, to the effect that I was overlooking the fact that animal passage makes infections more virulent, which accounted for the more rapid death after the first implantations in the case which was under discussion: namely, where I had drilled several small openings through to the interior of the tooth to permit more free exit of the toxic and bacterial substances. (See Chapter 17, on Quantity, Systemic Effect, and Tooth Capacity.)

The mesial root was again planted beneath the skin of a rabbit and it died, spontaneously, in five days; and still another implantation was made and the rabbit died in four days. Each one of the rabbits developed, besides the large subcutaneous abscess, such lesions as hyperemia of the myocardium, liver, and kidneys, acute myositis and atrophy of the chest and abdominal muscles, all with emaciation. The four rabbits into which the mesial root was planted lived on an average six and one-half days and had an average actual loss in weight of 256 grams, or 20 per cent, and an average loss per rabbit per day of 3.3 per cent. The two rabbits treated by planting the distal root, subdermally, died spontaneously in an average of thirty days, with an average loss of weight of 478 grams, or 31 per cent, or 1 per cent per rabbit per day.

The mesial root was then boiled for ten minutes and placed under the skin of a rabbit, which rabbit is still living at the time of this writing, fifty-one days after implantation. Apparently, the boiling did something to this tooth, for, whereas the other rabbits failed rapidly and died apparently from the effect of having this tooth implanted, this rabbit has gained from 852 grams to 1080 in the fifty-one days, a total gain of over four grams per

day. This rabbit, therefore, has had a gain of weight of 21 per cent in fifty-one days, or 0.4 per cent per day. It should also be noted that this rabbit had the same surgical shock that the others did. I desire to warn that it is not fair to conclude, however, that this method of treating suspected teeth—namely, to remove them and boil them and replace them—will always be as adequate as this, since, as I have shown elsewhere, these teeth often contain a toxic substance which is thermostabile and which continues to do some, though less, injury even after the tooth has been boiled.

These facts strongly suggest that the structure that is built about the root of an infected tooth is not a neoplasm, but that it is a protective membrane placed there by Nature to maintain a quarantine and thereby protect the animal or person carrying it. With this in mind, we have made a careful analysis of the condition of this tissue about the root apex in the various types of individuals presenting, and we have found that the type of tissue shown in Figure 198 of this chapter, is practically always present in individuals without rheumatic group lesions or apparent systemic affect from dental infections which they are carrying; and that if this normal high defense which has enabled them to produce this type of quarantine has been broken, there is a definite degeneration of this organ surrounding the apex of a tooth, and it takes on a condition such as that shown in Figure 197, which is the typical clinical state of the granuloma as found in individuals with a broken defense; and, further, that in those individuals, who have a chronically low defense, there is never an ample effort made to build such a quarantine station about the tooth. It is not well organized nor extensive in quantity, and we frequently, if not generally, find free organisms between this tissue and the root end. This type is illustrated in Figure 199. From a bacteriological standpoint in the individuals with either a chronically low defense or a recently acquired loss of defense (those with acquired susceptibility), we not only have the lack of well vascularized defensive tissue, but we have the definite evidence of infection in the form of organisms and very few phagocyted leucocytes; whereas in the periapical tissues of the individuals who have at that time an ample and high defense, we not only find a complete absence of organisms, but we do find both a highly vascularized tissue and the tissue elements necessary for an active defense: namely, many leucocytes, some of them phagocyted.

An illustration of one of Nature's mechanisms is shown in Figure 198-A and B. This shows in A the relation of the periapical defensive tissue to the root apex. It will be noted that there is little depression in the granuloma just over the exit of the apical foramen. This is shown highly magnified in B; and it will be noted that it is lined with a vigorous membrane of columnar epithelial cells, each with a well defined nucleus, and all of which have taken the stain vigorously, showing evidence of splendid vitality; and this seems to be the first line defensive tissue, for it is the type of tissue that Nature has built throughout the alimentary tract to defend us against the absorption of bacterial toxins. It is not strange that Nature should use the same effective mechanism here which she does in that extensive portal for bacterial and toxic entrance into the system.

If, then, as these data suggest, the dental granuloma so-called is not a neoplasm—in other words, is not a pathological tissue but a physiological tissue, whose function is to defend the individual against bacterial and toxin invasion,—we should have evidence of this quality by other means of observation. To test this I have placed various types of granulomata in both suspensions of organisms and freshly infected culture media with the remarkable result that whereas in the tube with the degenerating granuloma there is very little power to destroy bacteria in its vicinity, the vigorously functioning, freshly removed granuloma destroys the organisms in its vicinity in its tube, or at least there is developed a clear space in infected culture media for some distance surrounding the granuloma tissue. A bacterial count of the total fluid in the tube with the well organized granuloma shows a reduction from one-half to one-third that of the control tube.

A vigorously functioning granuloma should develop about the root of a tooth, carrying either a considerable quantity or a very toxic infection, such quantity as develops in practically any tooth providing the capacity of the dentin for bacterial growth and in addition the pulp chamber; and any patient who has this quantity of infection and does not produce such a defensive mechanism is not only in danger of being early affected, but in most instances is already being affected by the contents of that tooth. Such a condition is shown in Figure 206. This patient has carried this tooth for years. It has a fistula and he is in splendid health.

It is a most remarkable fact that when we study our old people who have lived through all the overloads incident to life and ex-

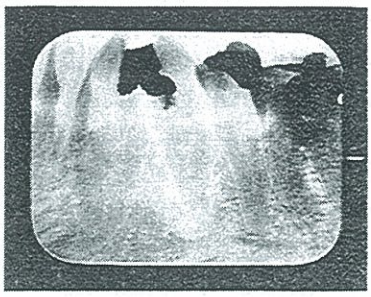


FIGURE 206. A VIGOROUSLY FUNCTIONING GRANULOMA IN A PATIENT OF A HIGH DEFENSE.

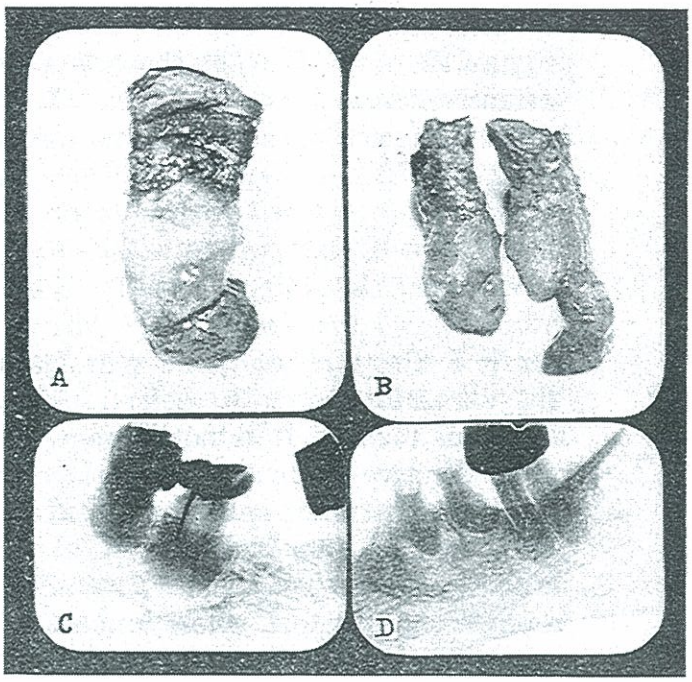


FIGURE 207. THE ROENTGENOGRAPHIC AND PHOTOGRAPHIC VIEWS OF GRANULOMATA WHICH PROTECTED THE PATIENT UNTIL ABOUT EIGHTY YEARS OF AGE.

tensive dental infections, and who in spite of them all and, particularly, in spite of what seemed to be extensive dental infections, are still well or relatively so for their age, we find this type of reaction about the roots of teeth. Such a case is shown in Figure 207. This patient, about eighty years of age, has several such teeth as this. C and D show the roentgenographic appearance of these two teeth, the lower right second molar and lower left second molar. Throughout her lifetime she has never suffered from neuritis, rheumatism, or nervous breakdown; and, incidentally, those disturbances are practically unknown in her family. A full set of roentgenograms of her case and also her brother's is shown in Figure 34 Chapter 3. When we study these teeth in connection with Nature's quarantine—namely, this vigorous, well vascularized, periapical encapsulation,—we see why she has had her protection. Incidentally, however, she has developed recently a kidney irritation which has entirely disappeared with the removal of these dental infections. Even her splendid defense has lately been breaking.

We do not yet know the full meaning and function of the epithelial structures which Nature builds into these highly efficient quarantine stations, but it seems very evident that it is not acci-

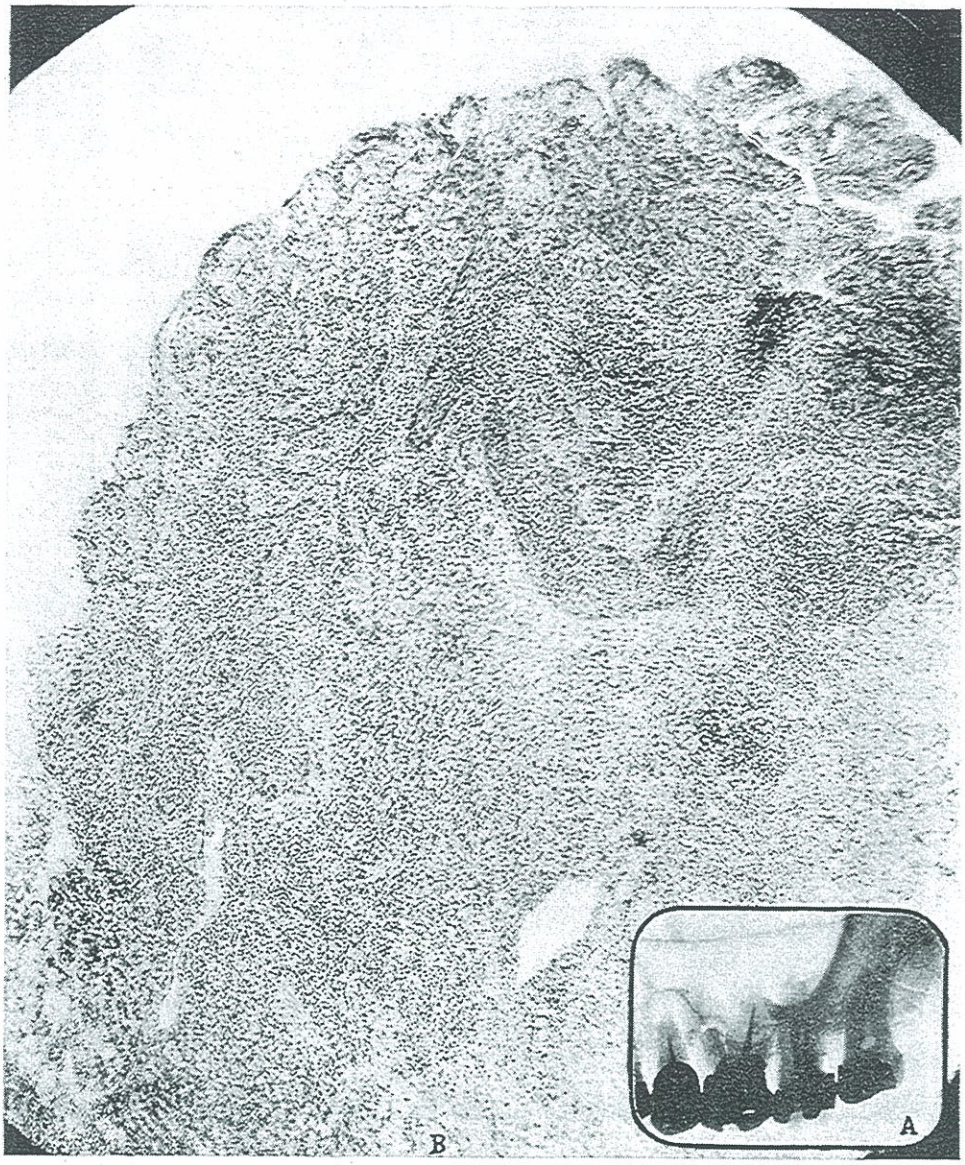


FIGURE 208. A HIGHLY FUNCTIONING GRANULOMA. NOTE THE LARGE AMOUNT OF EPITHELIAL TISSUE.

dental that this structure, when most efficient, carries a very large amount of epithelial tissue. This is illustrated in Figure 208, which is from the tooth of a patient with exceedingly high defense, the roentgenographic view of which is shown in A. It should not be presumed, therefore, that those individuals, having a high defense, as expressed by their capacity to build an efficient quarantine station about an infected root, are safe both for the present and future. To test this I have planted teeth in rabbits,

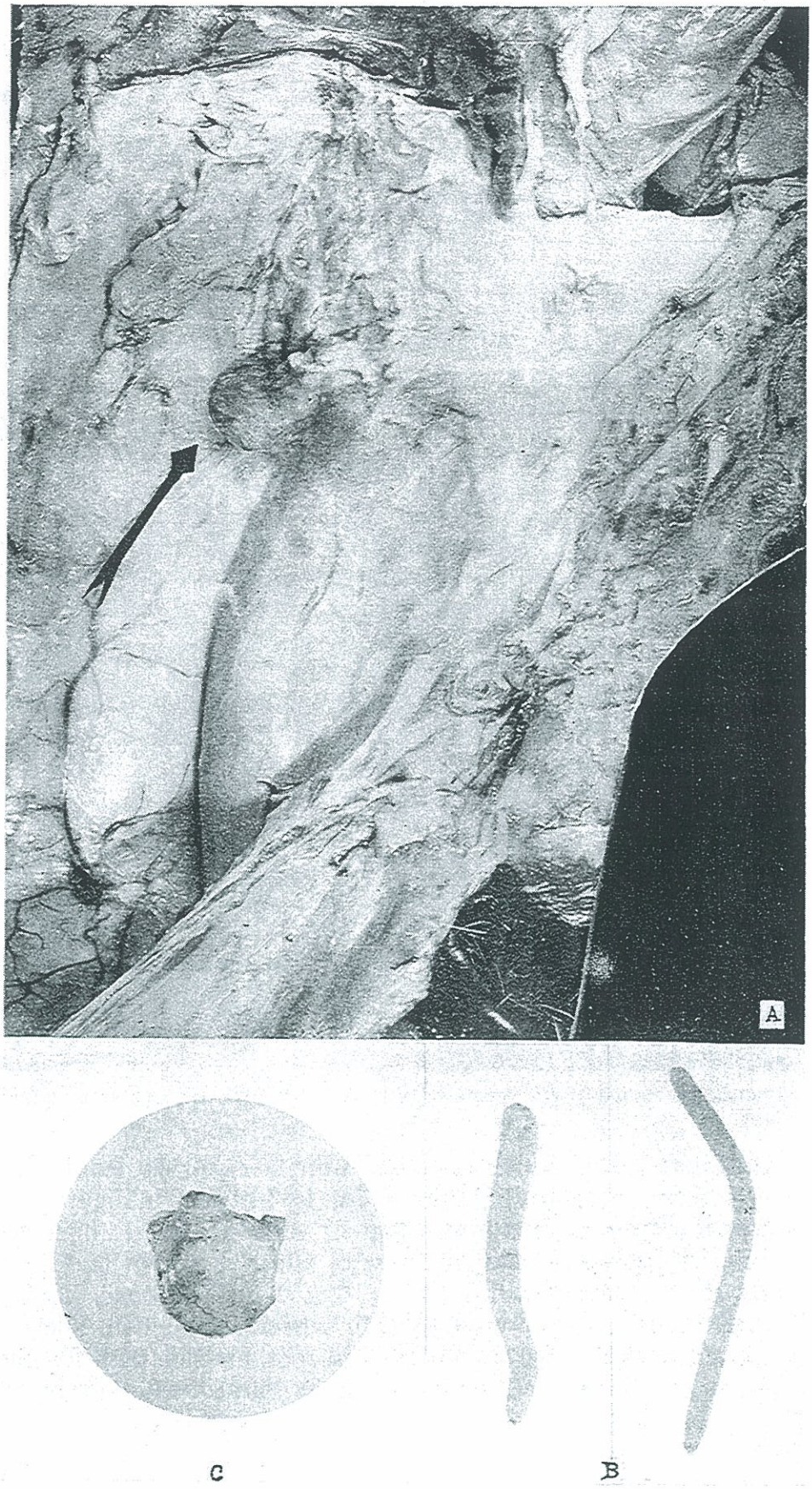


FIGURE 209. AN IMPLANTED TOOTH WHICH THE RABBIT CARRIED THIRTEEN MONTHS. IT DIED OF NEPHRITIS, FROM WHICH THE PATIENT WAS SUFFERING. C, THE ENCAPSULATED TOOTH; B, CASTS FROM THE RABBIT'S URINE.

and where they had built a high defense I have kept them under favorable conditions for long periods to see what the effects would be. Recently two of such test rabbits have died with nephritis, where the teeth had been implanted over a year previously and about which the rabbits apparently built adequate defense but in which contest the rabbit finally lost the fight. Figure 209 shows in A a dissection of a posted rabbit where a large broken down cyst is shown. It is remarkable that the animal gained from 975 grams

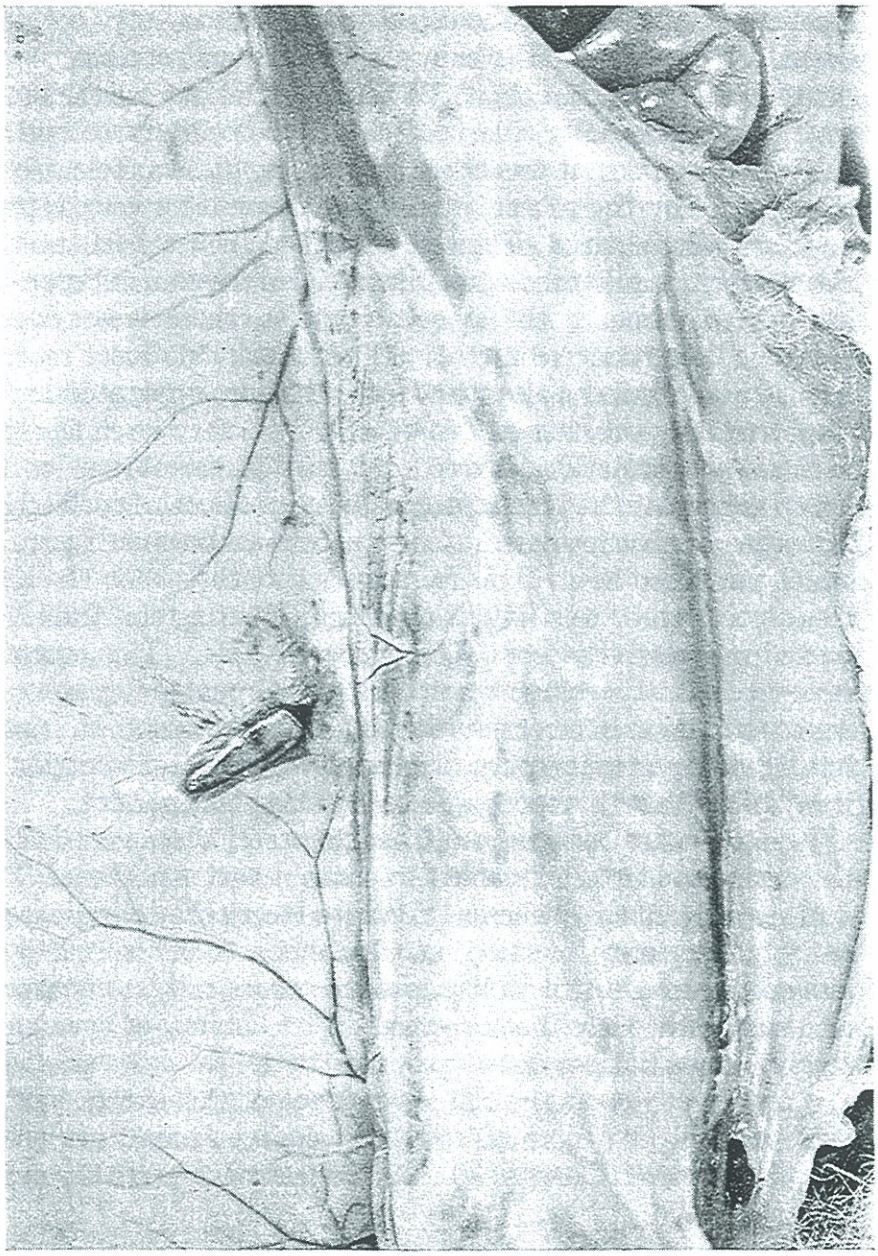


FIGURE 210. A STERILE IMPLANTED TOOTH WHICH PRODUCED PRACTICALLY NO ENCAPSULATION.

to 2885, nearly three times its original weight, in eight months, when it started to decline, and died thirteen months after the implanting of the tooth, with a weight of 2010 grams, having lost from its maximum weight 875 grams, or 30 per cent. Figure 209-B shows casts from this rabbit's urine, and C shows the encapsulated tooth. It is important to note that this patient was suffering from acute Bright's disease at the time of the removal of her tooth.

It is very important to note the very great difference in the local structural changes about a tooth which may stay for a long period of time under the skin of a rabbit and produce no evidence of injury to the rabbit. Whereas in the last case the tooth, which was potentially able, we believe, to do injury to both the patient from whom it was taken and the rabbit, was tolerated for a long time by the rabbit, it had built about it a very vigorous and well vascularized defensive tissue. When sterile, non-irritating, foreign substances, as illustrated in the coin in Figure 201, are planted beneath the skins of rabbits, there is not only no systemic disturbance, but there is practically no local reaction. This is what happens also when teeth that are implanted are free from irritating substances. In other words, they lie in the tissue without encapsulation, covered only with a membrane so thin and transparent that the tooth can be seen almost as perfectly as if it were not encapsulated. Such a tooth is shown in Figure 210, which remained in a rabbit for sixteen months, when the rabbit was chloroformed to study its structure. During this time it had gained progressively from 1603 grams to 3034. This tooth was removed from the patient not because of roentgenographic evidence that it was in error but as a matter of precaution, the patient having had a serious injury from a previous dental infection. It is my belief that this tooth was not injuring this patient.

In a previous paragraph of this chapter I discussed the fact, that even boiled teeth seemed to contain toxic substance. It is quite important that, whereas implanted teeth that are apparently entirely free from infection, such as some of our surgically removed impacted third molars, produce practically no encapsulation such as the last tooth showed. The boiling, or even autoclaving, of teeth does not always destroy all the toxic substance. We do not yet know the full significance of this except that the toxin seems to be thermostabile and we have found evidence of this, (as shown in Chapter 30 on Sensitizations, where the extract

taken from teeth was found to produce the typical intradermal skin reaction) in many instances, each when passed through a Berkefeld filter, when sterilized chemically, when boiled for an hour, when autoclaved at thirty pounds, and also when autoclaved at three hundred twenty pounds for two hours. I was, therefore, not surprised to find that there was a distinct difference in the reaction locally and on animals when boiled teeth had been infected. Boiled and autoclaved infected teeth have encapsulations developed about them almost invariably. But this is not the most important part of it. Very often the rabbits carrying these teeth show blood changes within a couple of weeks and begin losing in weight. Figure 211 shows the typical appearances of the

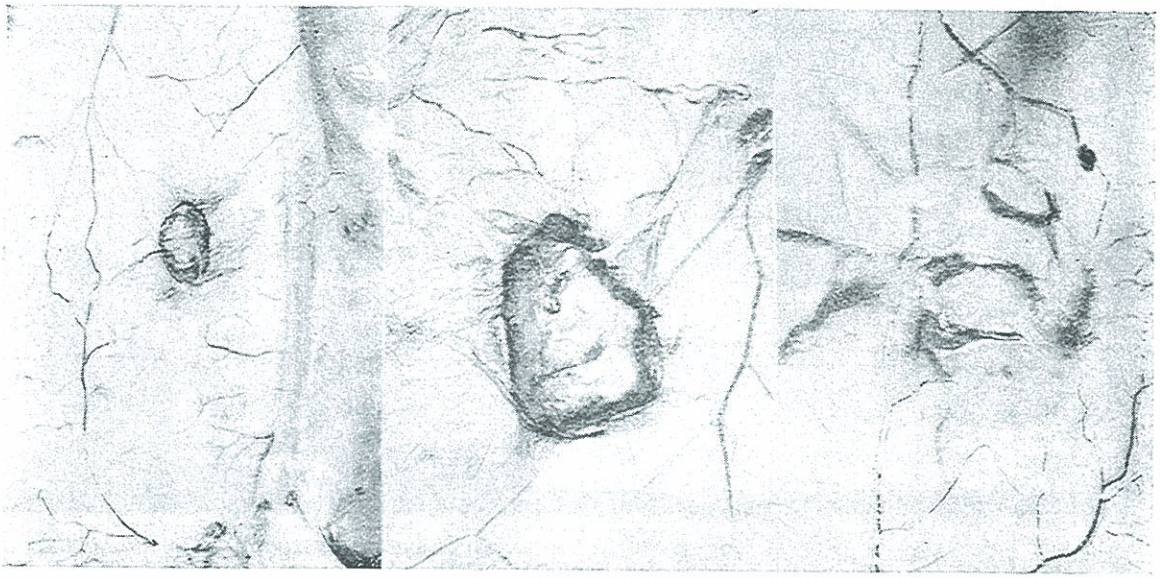


FIGURE 211. ENCAPSULATIONS ABOUT BOILED INFECTED TEETH. HEATING DID NOT DESTROY THE TOXIN.

encapsulations about three such boiled teeth. A was boiled for one hour. The rabbit (No. 1165) died in twenty days, with a loss of 160 grams, or 9 per cent. It is impossible to state definitely to what extent the tooth contributed to the rabbit's death. B (Rabbit 1189) died spontaneously in twenty-two days, with a loss of 149 grams, or 15 per cent. The tooth was boiled for two hours. C was autoclaved at thirty pounds pressure for one hour. This rabbit (No. 1171) was chloroformed in six days, as it was nearing death, with a loss of 332 grams, or 31 per cent. It is therefore apparent that these infected teeth contain a substance which has a direct action on metabolism. This rabbit, having

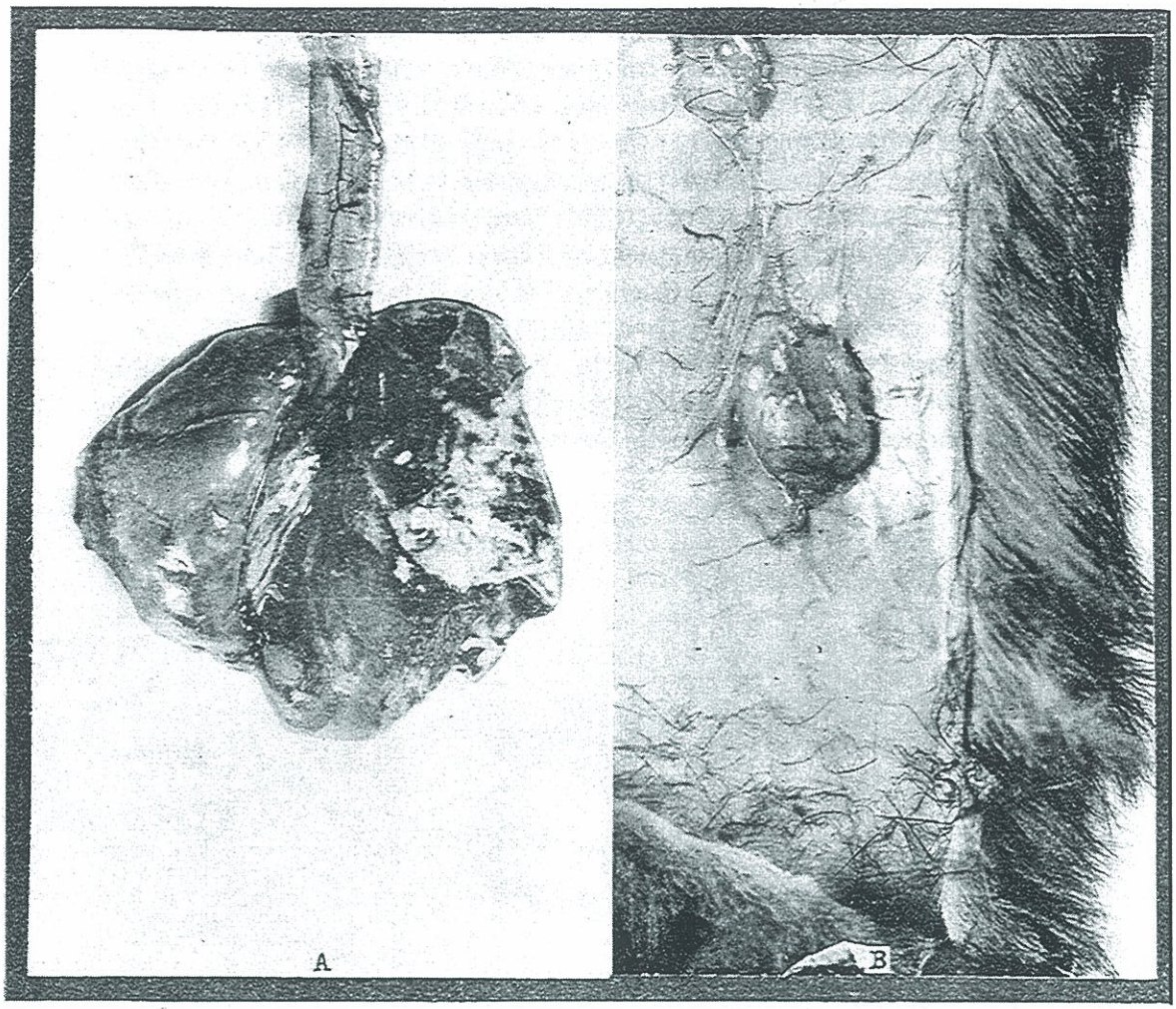


FIGURE 212. ONE OF SEVERAL RABBITS WHICH DEVELOPED PNEUMONIA FOLLOWING THE IMPLANTING OF AN INFECTED TOOTH. A, PNEUMONIC LUNG; B, THE ENCYSTED TOOTH.

lost this large amount, was rapidly approaching death; and, in order to secure the blood before any postmortem changes could take place, it was chloroformed; and while under chloroform before death, sufficient blood was aspirated from the heart to make our blood calcium determinations. In this rabbit the ionic calcium was approximately normal, 10.7, and it, apparently, had not undergone the same structural changes of the blood that those rabbits did which had this same tooth planted beneath their skins before it was boiled but with its normal infection as taken from the patient.

A further and striking evidence of the toxicity of these infected teeth and of the nature and stability of this toxin, is shown in the fact that frequently the rabbits carrying these implanted teeth die of pneumonia. Such a case is shown in Figure 212. This

rabbit had a tooth planted which had previously killed several rabbits by subcutaneous subdermal implantations, but before this implantation it was autoclaved for one hour at thirty pounds. The rabbit died in thirty-five days and lost in weight 617 grams, or 36 per cent.

It may be argued that in these cases the heating to high temperatures has produced a protein compound that is irritating or poisonous. To test this further we have heated a tooth to 56° for one hour. This should not produce structural change in the protein molecules sufficient to be toxic, and should destroy non-spore forming organisms, which would include the streptococcus. This rabbit died in eight days, with fibrous encapsulation, as shown in Figure 213. It lost 145 grams, or 16 per cent.

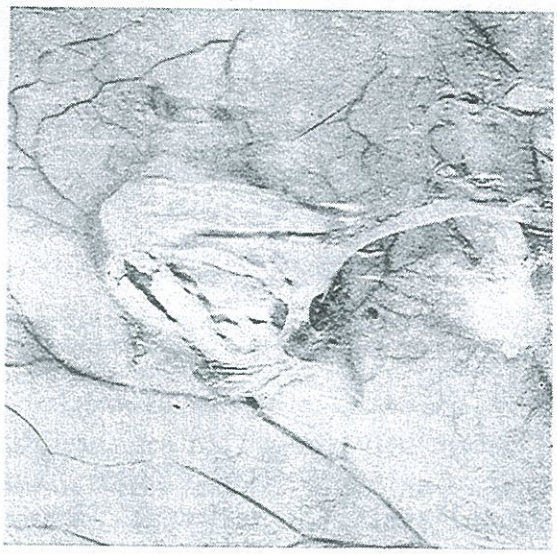


FIGURE 213. TOOTH WAS HEATED TO 56° FOR ONE HOUR BEFORE IMPLANTATION.

The so-called granuloma, for this seems clearly a misnomer, has apparently in these cases destroyed a large number, and in some instances a large proportion, of the bacteria present. To test this further we have placed pieces of such granuloma taken from healthy individuals on agar plates, which had first been inoculated by flowing over their surfaces a suspension of bacteria and pouring off all excess. As shown in Figure 214, while the organisms grew in massive colonies all over the plate, practically no organisms grew for several millimeters surrounding the granuloma, notwithstanding the fact that we might readily expect that its bacteriolytic action should only be available during the time of its vitality.

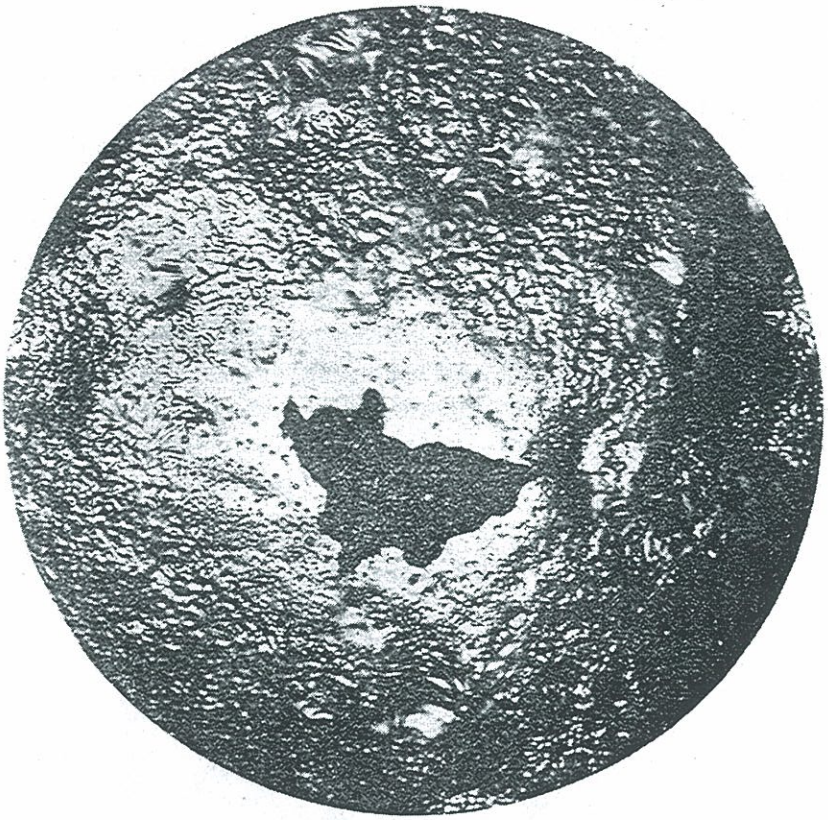


FIGURE 214. SHOWS THE REDUCED BACTERIAL GROWTH IN THE VICINITY OF A WELL ORGANIZED GRANULOMA WHEN PLACED ON AN INFECTED PETRI DISH.

SUMMARY AND CONCLUSIONS.

We would, accordingly, change our interpretation and evaluation of that structure which Nature builds about a root apex. With these data in mind, let us review the findings of Chapter 3 in which, in many instances, the same infection produces an entirely different structural change about a root apex, to what it does in others; and in Chapter 4 that there is a great difference in the susceptibility of individuals to injury from dental infections; and particularly in Chapter 5 that it is those individuals with the large area of rarefaction about the tooth, and hence a large so-called granuloma, who prove to be the persons who, as shown in Figure 200, have a high defense or are free from danger

from injury from their dental infections. Since, then, (1) these large areas, as is continually shown in surgical procedure in removal of teeth, contain a more abundant defensive membrane, which type of membrane Nature reproduces in the rabbit, if that same tooth be placed beneath the skin, and thereby protects the rabbit from the toxic substance within the tooth; and (2) since the blood changes as expressed in ionic calcium vary in direct proportion to the ability to build such a membrane, we find no alternative from the following conclusions:

(1) The so-called granuloma is a misnomer, for it is a defensive membrane and not a neoplasm.

(2) A normally functioning periapical quarantine tissue is Nature's effective mechanism for protecting that individual by destroying the organisms and toxins immediately at their source, and thereby completely preventing the tissues of that individual's body from exposure to either of these agencies.

CHAPTER XXXIX.

CHANGES IN THE SUPPORTING STRUCTURES OF THE TEETH, DUE TO INFECTION AND IRRITATION PROCESSES.

EXPERIMENTAL AND DISCUSSION.

In the preceding chapter, the data have disclosed a wide variation in the structural changes which occur in the supporting structures of the teeth, depending upon the nature and quantity of the irritant or infection, and the capacity for defensive reaction on the part of the individual. In Chapter 3, we saw that either, or both, a rarefying osteitis or a condensing osteitis may be produced about the apex of a root of a tooth; and in Chapter 5, we found that the condition expressing itself in very extensive destruction of bone about the apex of a root, occurs in individuals with a high defensive reaction against the dental infection; that in these individuals, during the time of their high defense, the zone of rarefaction blends into the medullary spaces in a diffuse manner; that when these individuals lose this high defense, the zone not only ceases to become larger, but a fistula, if present, tends to become closed, and a zone of condensing osteitis tends to develop around the zone of rarefaction; and that in those individuals with a low defense for the type of infection always found in dental lesions, streptococcal diplococcal types, not only low at present but for a long period previously, the condition resembles that of the last type except on a much smaller scale in that the zone of rarefaction is usually very much smaller, for a given infection, while the zone of condensation may be very much greater.

I have undertaken to discover somewhat more in detail the nature of these processes, and in order to do so have made extensive dissections of a large number of maxillae and mandibles. A typical illustration of what we have just reviewed in the preceding is shown in Figures 215 and 216, which show in 215 a mandible with two bicuspids and three molars in place, with the buccal plate removed. A couple of metallic wires have been placed through the inferior dental canal, passing out through the mental foramen.

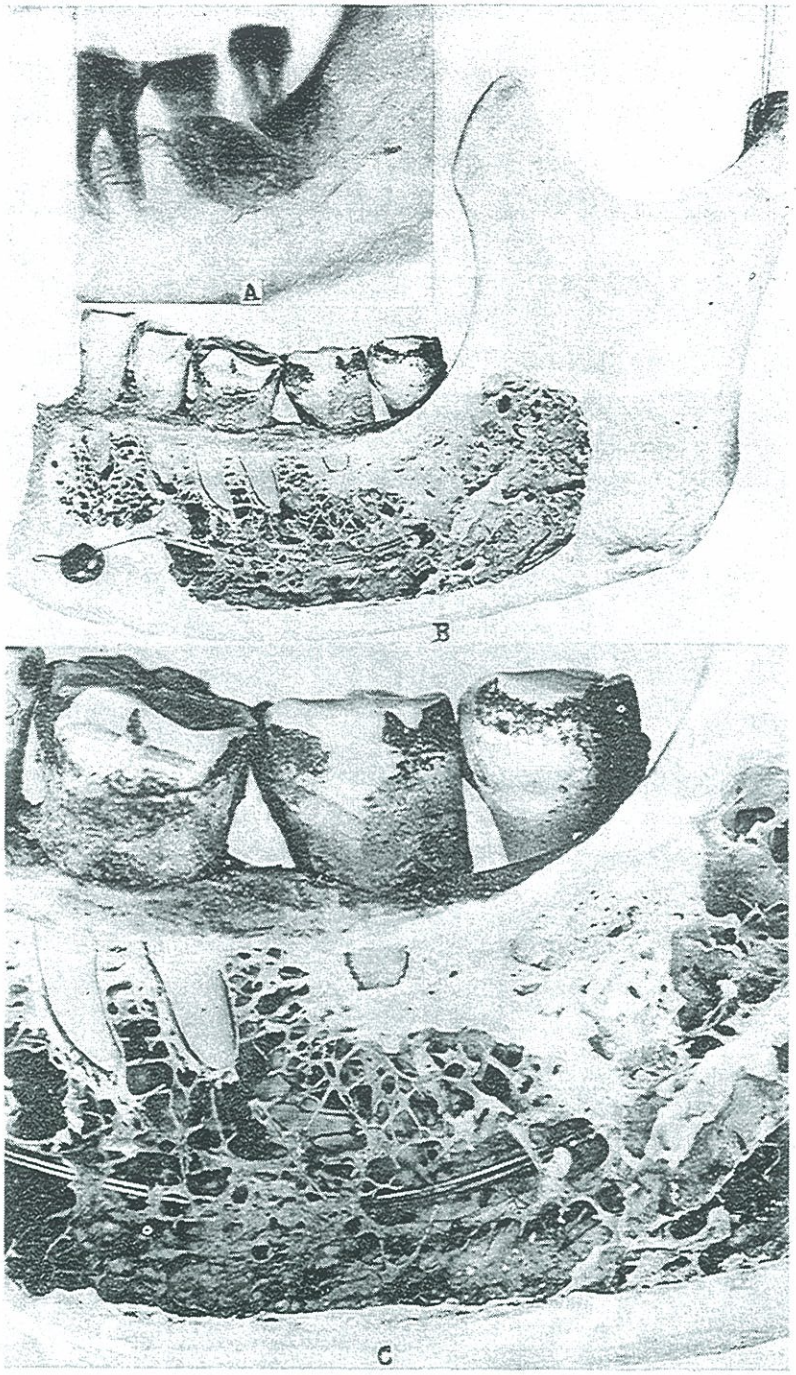


FIGURE 215. A, THE ROENTGENOGRAPHIC APPEARANCE OF THE DISSECTIONS IN B AND C. NOTE POCKET BETWEEN SECOND AND THIRD MOLARS AND ADJOINING RADIOPACITY. B AND C SHOW THE ARRANGEMENT OF THE CALCIFIED STRUCTURES.

Figure 216 shows progressive enlargements of the normal and pathological bone about the molar teeth. (Note: In the various views of this specimen an artefact presents, seen in Figures 215-B and

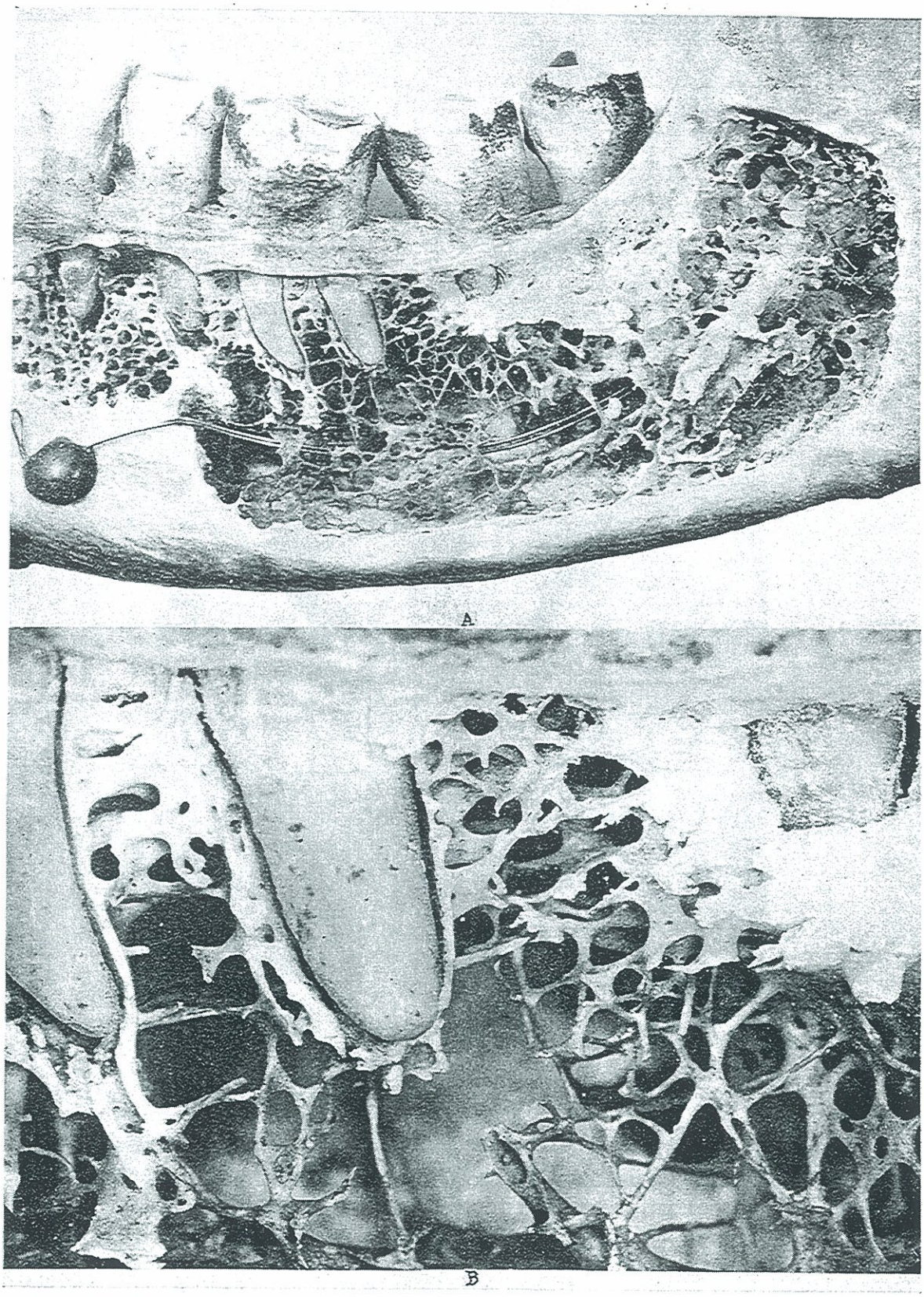


FIGURE 216. ENLARGEMENTS OF PRECEDING TO SHOW TRABECULAR ARRANGEMENT AND CONDENSING OSTEITIS SURROUNDING A PERIODONTOCLASIA POCKET. A LATE STAGE.

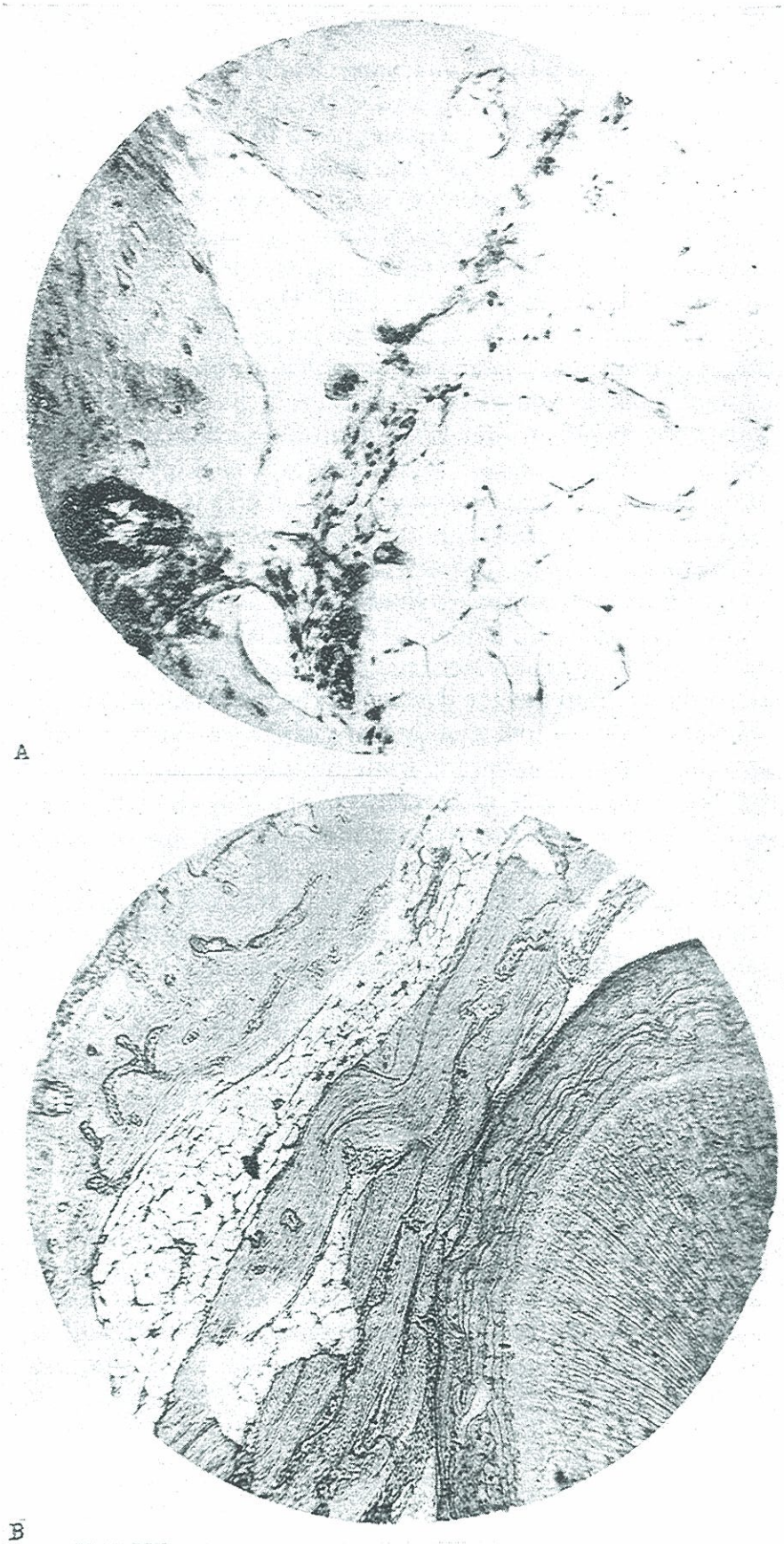


FIGURE 217. A, OSTEOCLASTS IN THE PROCESS OF REMOVING ALVEOLAR BONE IN PERIODONTOCLASIA. B, A CROSS SECTION OF THE TOOTH AND SUPPORTING ALVEOLAR BONE.

216-A. When the tissue was being cleaned the bicuspids were dislodged and were cemented back without care being taken to have them properly seated. What appears to be areas of absorption about the apices of the two bicuspids are open spaces due to the fact, that the teeth are not receded properly in their sockets. There is no pathological absorption; the original lamina dura is present.) Several things will be noted: First, the very porous condition of the normal bone below the bicuspids and first and second molars, and the very dense bone, amounting almost to a homogeneous mass, below the second and third molars. A more careful examination of this case reveals, as shown in the roentgenogram in 215-A, that there is an old periodontoclasia pocket mesial to the third molar, where food was packing; and my interpretation of the condition would be, that this individual's defense had reduced a considerable time before his death; and that with this lowered defense, the active spirochete infection in the periodontoclasia pockets, which had been a participant in the original destruction of the gingival crest and alveolar bone, had largely given way to coccal infections, particularly streptococcal, in the deep tissues, and bacillary forms in the periodontoclasia pockets. The effect of the irritation in the vicinity of this bacterial invasion was entirely different from the process that had occurred earlier in the history of this lesion. At that time, when the patient's defense was high, the cellular activity was so acute that with the stimulation of the irritation, all cell function was high. With the toxic irritation came a very marked dilatation of the capillaries. These poured out their defensive factors, which were markedly alkaline and contained large numbers of leucocytes. These defensive factors were quite ample to establish a quarantine about that local infection, thereby inhibiting the passage of either the bacteria or their products from entering the system. A part of this process involved the destruction of alveolar bone, for the fluids and cells poured into this part were those adapted for the tearing down of alveolar bone as fast as it became involved.

This process of decalcification is so often a physiologic one that it is difficult to distinguish between a physiologic and pathologic absorption of bone. An illustration of this process is shown in Figure 217, which shows in B a cross section of a tooth and the supporting alveolar bone, and in A the giant cells in the deepest part of the periodontoclasia pocket engaged in the process of taking

down the hard structures and transporting them in an absorption process. With the development of overloads, whether age, exposure, or disease, the defense of all individuals goes down; and in Figure 215, we see a zone of very dense bone where the trabecular structure is almost completely obliterated. If we would compare the bone formation about the roots of the first molar with that of the second and third molars, we would find a very striking difference. This is shown in higher magnification in Figure 216. Note that the lamina dura about the roots of the first molar is the thin shell supported lightly by trabeculæ of small size, which form almost a lace-like network in the body of the mandible. Note where a section of the cancellous osseous structure is broken out below the apex of the distal root of the first molar, that there is an open osseous channel exposed, through which the blood vessels and nerves entering the distal root of the first molar pass protectedly in a tube through the medullary matter up to the root apex. This condition is also shown in the osseous structures leading to the mesial root of the first molar.

The roentgenographic study of this condition is shown in A of Figure 215, and reveals the following: a zone of condensation or radiopacity about the second and third molars and a normal cancellous bone about the first.

Before proceeding with the discussion of these structural changes, I wish to call attention to the fact that, in preceding chapters, I have frequently spoken of the fact that teeth and their sockets of individuals with normally high defense, and particularly those with abnormally high defense, respond very differently in the various surgical procedures, operative and postoperative. For example, it will readily be seen why it would be very easy to infiltrate an anesthetic into the supporting structures of the bicuspids, while it would be relatively difficult in these molars; and also with a highly vascularized medullary fat filling the interspaces between the trabeculæ about the bicuspid roots, it would be exceedingly easy for Nature both to combat infection and repair tissue, as compared with her facilities and ease for carrying on that function in the case of the molar roots. The vascularization is gone, largely, in the latter case. It would be much more difficult to extract a root in this latter condition and it would readily be understood why the old process would be very much more delayed and interrupted in this latter condition; and, indeed it could easily be understood why Nature might desire to throw

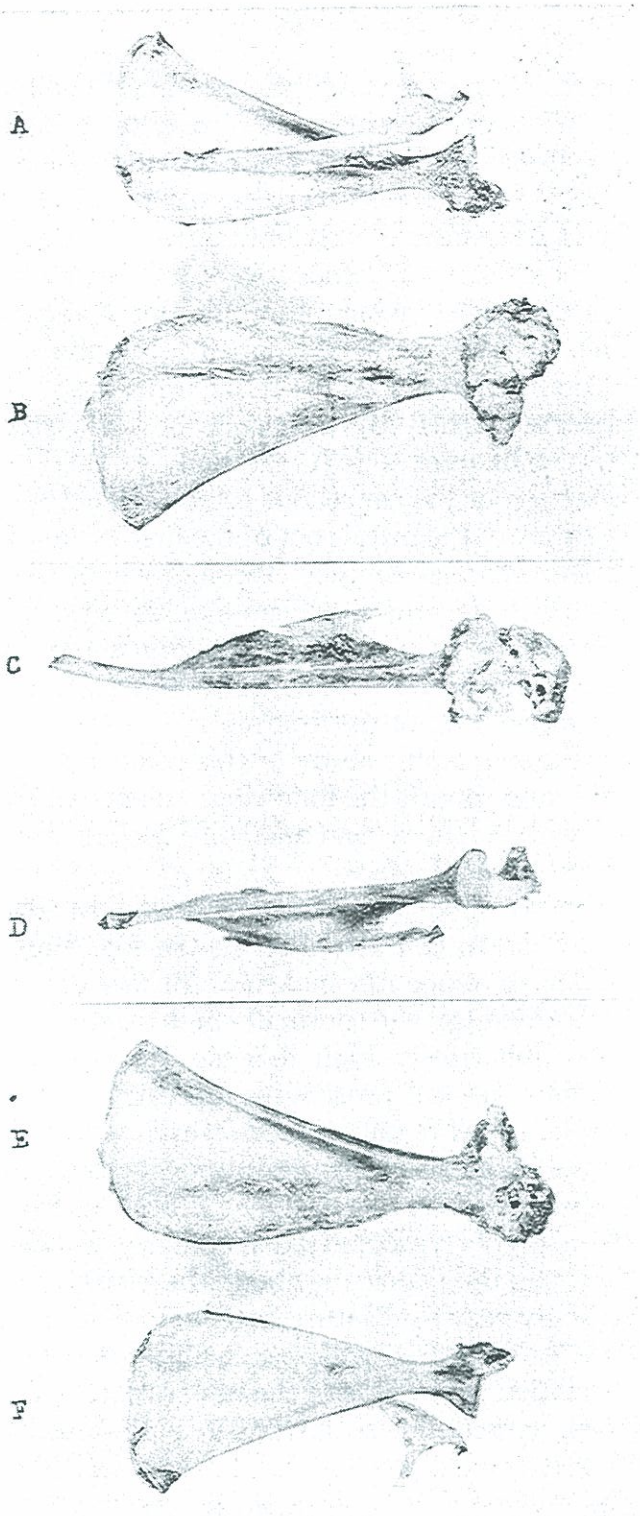


FIGURE 218. A PROLIFERATIVE ARTHRITIS IN A RABBIT'S SHOULDER. A, D, AND F SHOW NORMAL SCAPULAE; B, C, AND E GROSSLY DEFORMED.

off as a sequestrum a large or small part of this condensing bone.

But our process is not limited in this instance to the irritation of infection entering the original exposed and necrotic bone, for the presence of that infection has, as we have shown in Chapter 8 on Periodontoclasia and Pulp Involvement, in all probability, injured the pulps of these teeth.

There is another and very important phase of this problem which has not received proper consideration, which is the reaction of the infection from near or distant parts of the body on the supporting structures of the teeth. In the preceding discussion, we have almost entirely limited our considerations to the effect of dental infections on the immediate adjoining dental and supporting structures, and upon other tissues and organs of the body. Since a tooth is suspended in a socket in such a manner as to make a movable joint, it and its supporting structures are subject to many of the structural changes to which any or all joints may be susceptible. In order that we may understand, somewhat, the nature of this process, we will approach it by a consideration of the changes which take place in the joints. These may be, in general, divided into two main groups which we will refer to as degenerative and proliferative processes. Each of these will produce deforming arthritis. In the first there is marked ankylosis, lack of mobility, and with removal of the dental infection or other source of irritation which has been largely instrumental in furnishing the toxic and infective processes for its development, there may be a cessation of inflammatory process with fixation, a more or less permanent ankylosis, but often with quite complete freedom from pain. These individuals may live for years, not infrequently twenty or thirty, with many or nearly all joints of the body immobile. In other instances there is a slow reparative process. In the second group, with the degenerative arthritis, there tends to be a destruction of synovial membrane, with destruction of the cartilages and often with marked absorption of the bone. These two types are shown reproduced in rabbits in Figures 218 and 219. It is important to note that in our animal studies we have found that strains taken from some teeth tend quite regularly to produce in rabbits the former type, while strains taken from teeth of other patients inoculated into rabbits produce changes of the latter type. We will discuss this in further detail in a later communication.

A minute study of the pathological changes will be seen in the

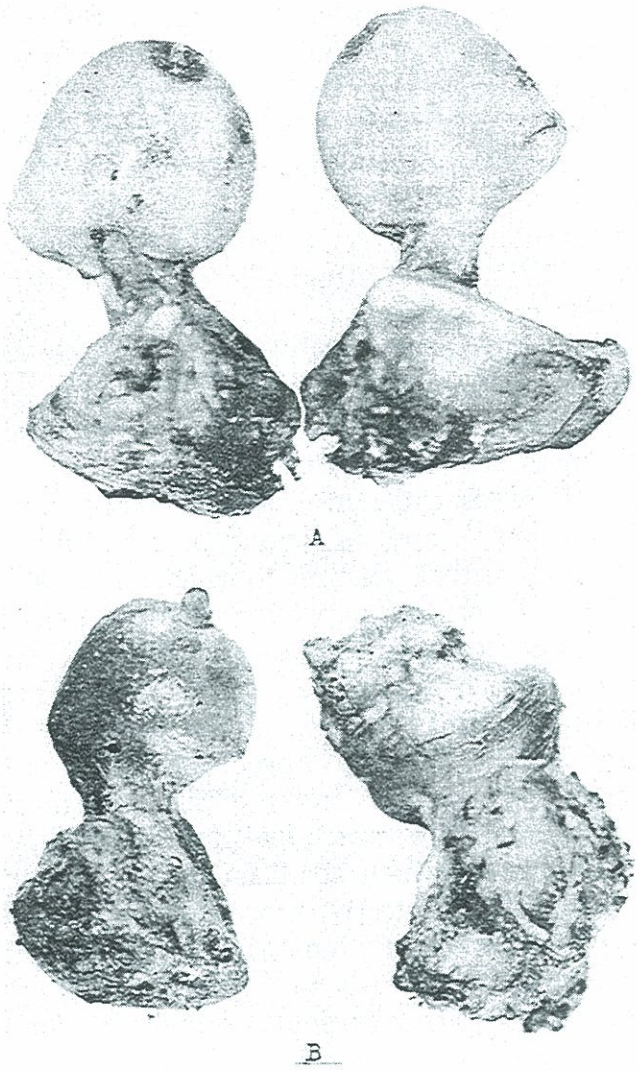


FIGURE 219. A DEGENERATIVE ARTHRITIS IN A RABBIT'S HIP JOINT. A, NORMAL HEADS OF FEMORAE; B, DESTRUCTION OF ENTIRE ARTICULATING SURFACE.

following figures. Figure 220 shows a section through the knee joint of a rabbit suffering from acute rheumatic infection resulting from a minute inoculation in the ear vein. It will be noted that the inflammatory process has attacked the trabecular structure and also the cortical layer beneath the synovial membrane. The synovial membrane is itself seriously attacked in some places, as shown in Figure 221. It will be observed that the degeneration is extending through this membrane into the cortical layer. The tissues of the knee shown in Figures 220 and 221, were cultured and a diplococcus was isolated which was also shown in direct

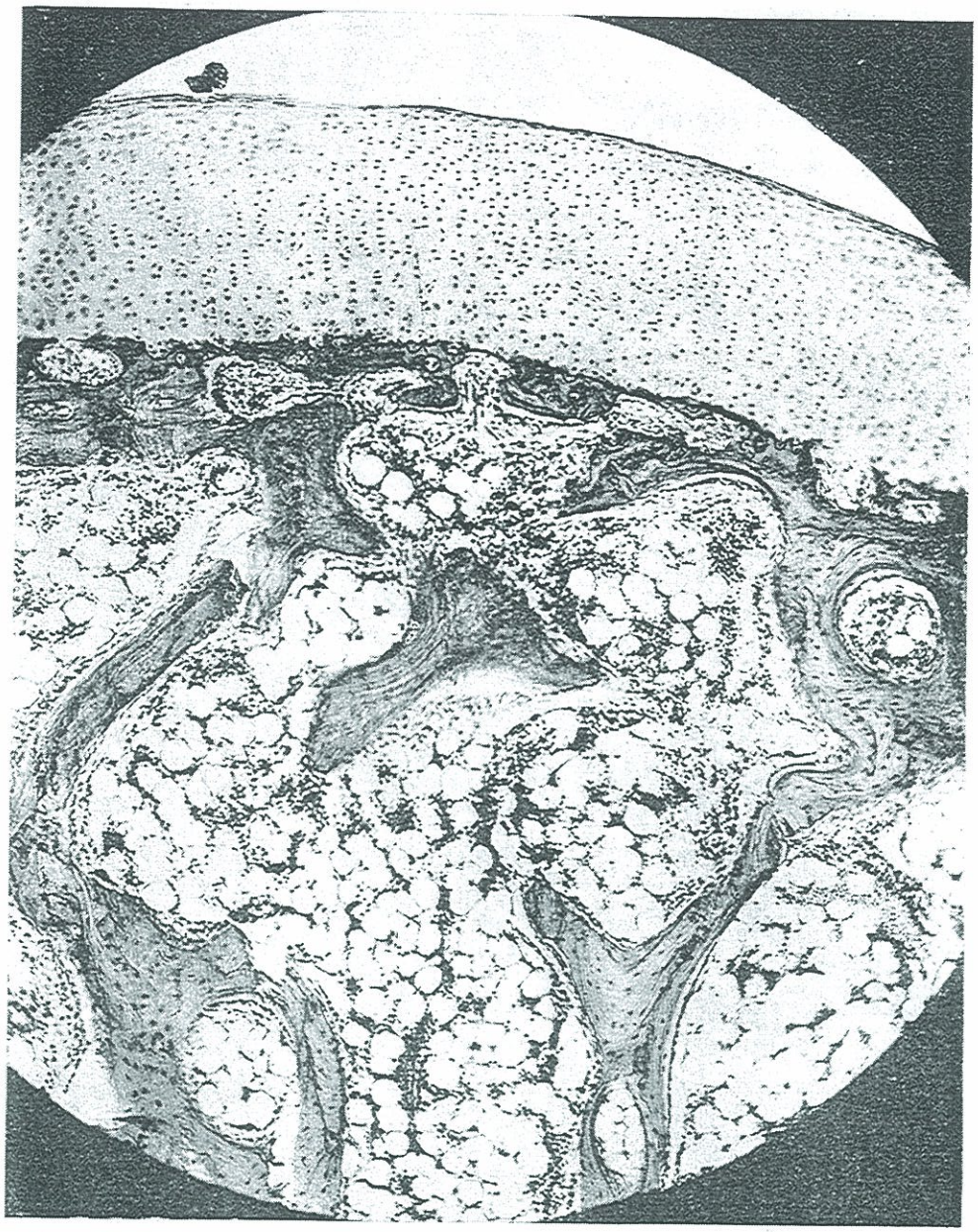


FIGURE 220. A DEGENERATIVE PROCESS IN TRABECULAE AND CORTICAL LAYER OF A RHEUMATIC JOINT.

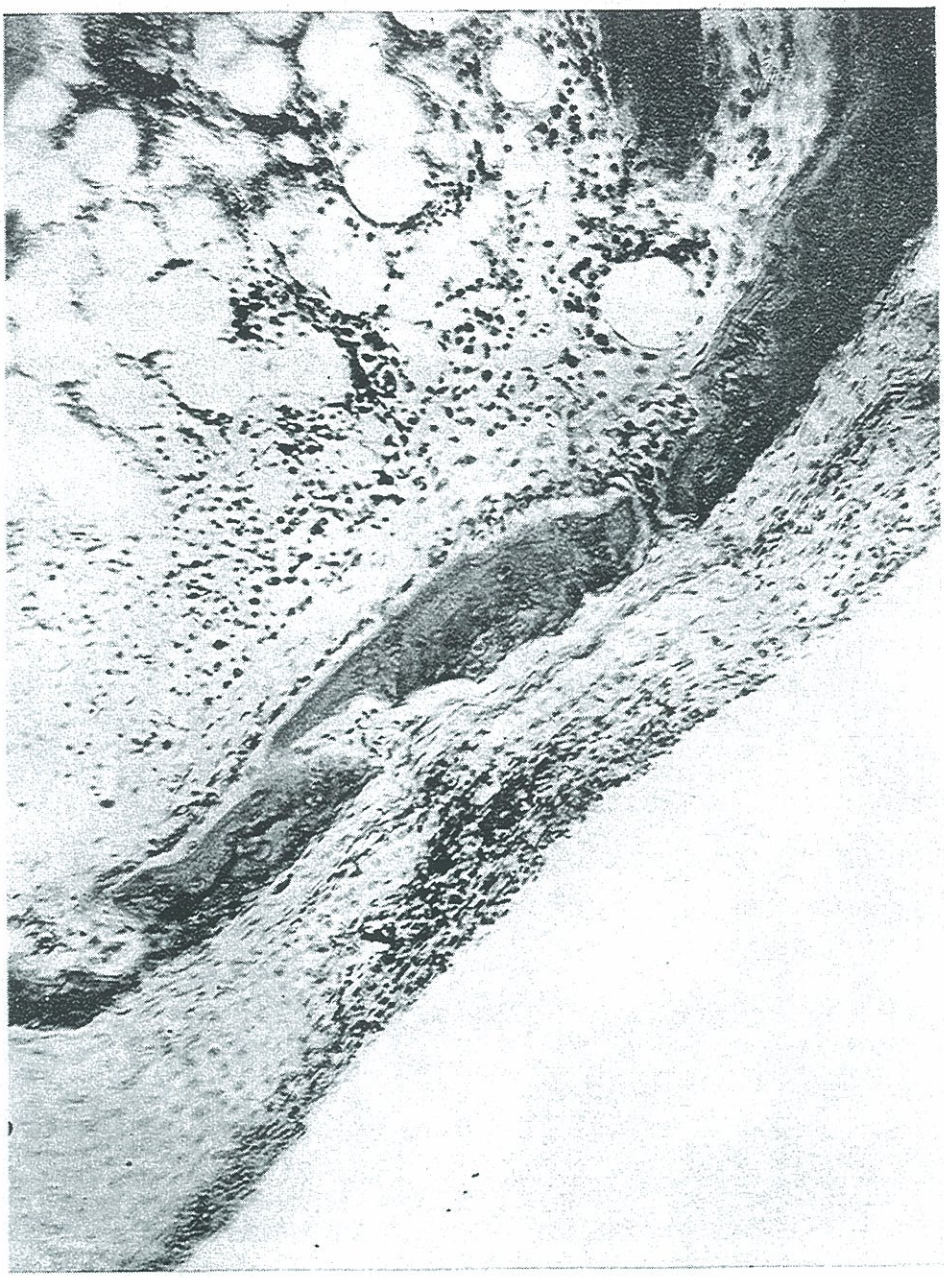


FIGURE 221. BEGINNING INFLAMMATORY PROCESS IN THE SYNOVIAL MEMBRANE.

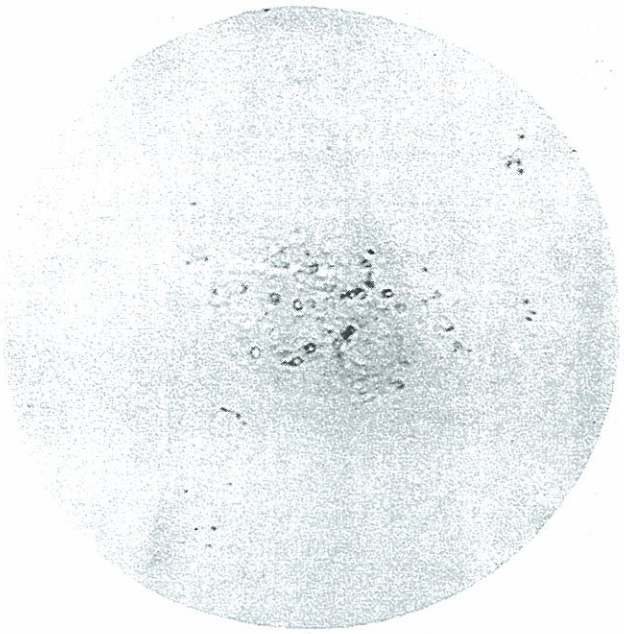


FIGURE 222. DIPLOCOCCI SEEN IN A SMEAR FROM A RHEUMATIC JOINT.

smear. These are shown both free and phagocyted in Figure 222.

Irritations of the peridental membrane which stimulate its cells to an osteoclastic reaction may produce changes in any adjacent hard structures. Consequently the processes which attack the alveolar bone frequently attack the cementum and even the dentin of the tooth. A most striking and interesting illustration of this is shown in Figure 223, in which instance a lateral tooth was under orthodontic treatment. As shown in 223-A, there was a large metallic filling on the lingual surface. Beneath the old metallic filling there was infected caries which had not been observed. With the addition of a little pressure on the tooth, an acute pulpitis developed; and since the case involved the movement of the cuspid, which was quite entirely outside the arch, it was deemed best to extract this lateral thereby to give available space for placing the cuspid without a long tedious operation of the movement of the molars and bicuspids. This gave us a very favorable specimen for study, a condition we had been looking for. B shows the low power view of a section of this tooth; and it will be noted that on the side receiving the pressure, the cementum is almost entirely removed. Attached to this side there were areas of peridental membrane, as shown in Figure 223-B. Two of these are

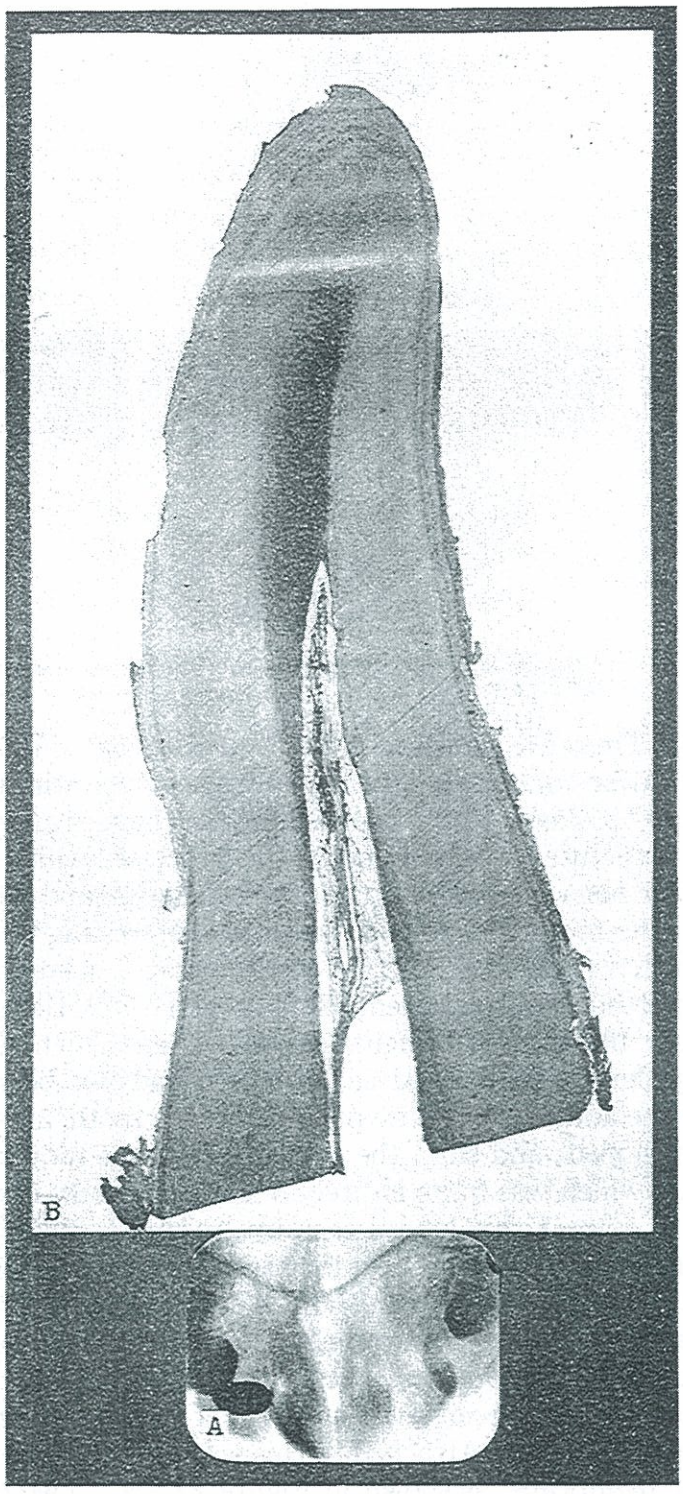


FIGURE 223. A CROSS SECTION OF A TOOTH UNDER ORTHODONTIC PRESSURE. NOTE ABSORPTION ON THE ADVANCE SIDE OF MOVEMENT.

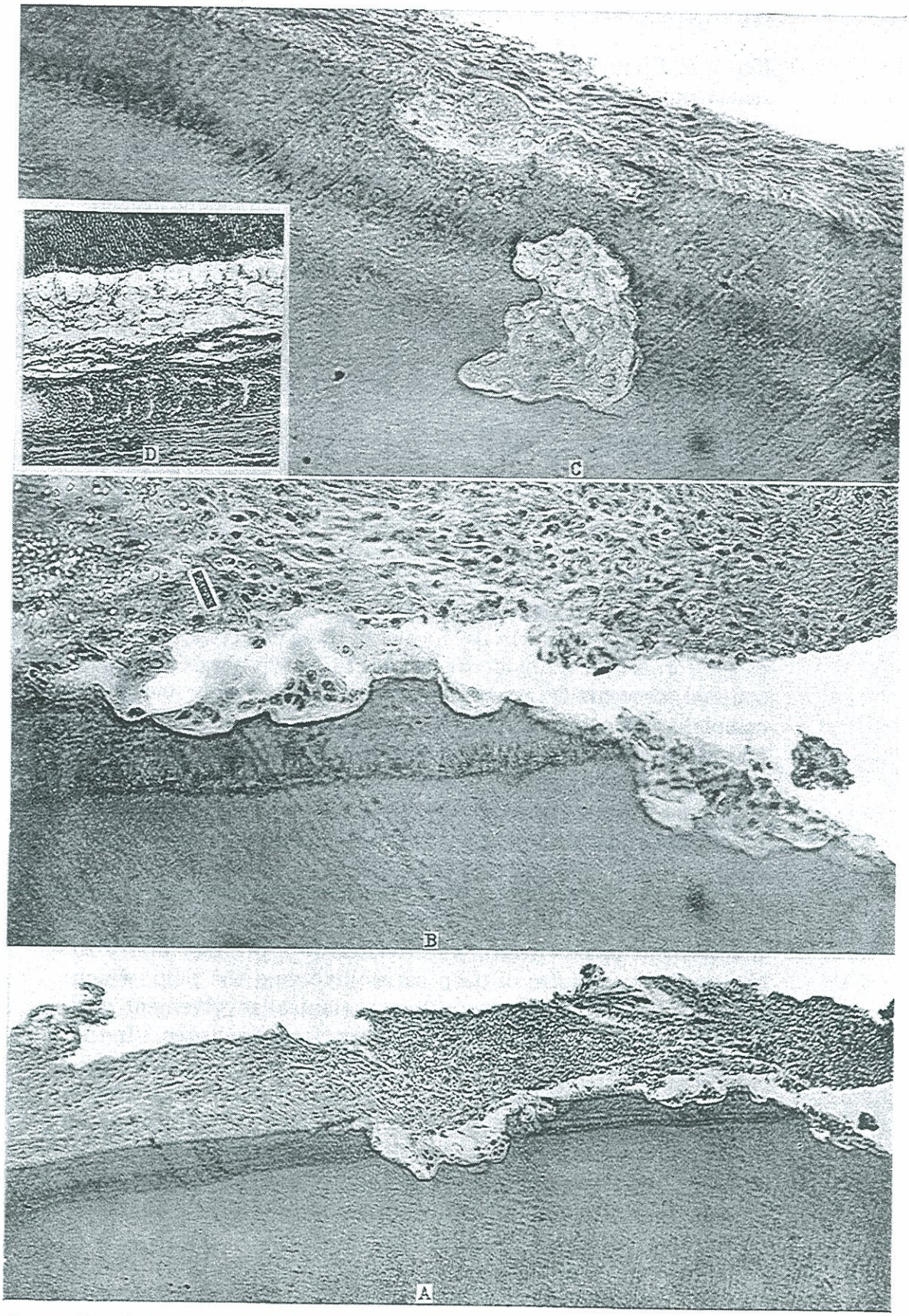


FIGURE 224. A, B, AND C, OSTEOCLASTIC ACTIVITY; D, HEMORRHAGE INTO PULP OF TOOTH OF PREVIOUS FIGURE.

shown in Figure 224-A and B, in which it will be observed that the cementum has been entirely removed in places and the process is proceeding into the dentin. The osteoclastic cells are clearly shown in the process of removing this structure. It is also important to note that this process has extended in some places deep into the dentin. A section across one of these burrowing excavations is shown in Figure 224-C. Either due to the toxic materials from the caries or to the mechanical trauma of the orthodontic process, or both, there was developed, as previously stated, an acute pulpitis. It is exceedingly interesting to note that there were profuse hemorrhages into the pulp tissue which, apparently, had previously been undergoing a process of fibrosis. This is shown in Figure 224-D.

When we study clinically some of our patients who have had deforming arthritis for years, we find that not only is there evidence of the most indisputable type that the dental infections have contributed directly to the development of the arthritis, but there is just as indisputable evidence that some of these individuals have had characteristic degenerative processes produced in their teeth, which were not otherwise involved, by their general rheumatic condition. In the former of these two conditions, one of the forms that the evidence takes is that individuals who have suffered for years from acute or subacute processes, have had complete and continued relief from the recurring exacerbations, and a change of their general state from one that had been getting progressively worse to one that became progressively better; and this same history had repeated itself in the same individuals by the subsequent involvement of other teeth, followed by a return of their acute processes, all tending to a return toward normal with removal of the dental infections. But note, in these cases these changes, which developed following the involvement of new teeth, were related to a primary injury to the tooth in the form of deep caries involving the pulp, which developed in the regular sequence, periapical involvement, and degeneration and irritation of the supporting structures. In the latter of these two conditions—namely, where the arthritis produces injury and degenerative processes in the teeth—we have found these degenerative changes, first in the peridental membrane, and then in the pulp, without the approach of caries or any apparent evidence such as will ordinarily be found requisite to produce a destruction or change in the dental pulp. To cite a

specific case, one of the arthritic cases that I am watching very closely has in five years had six teeth come to have non-vital pulps, or definitely involved and infected pulps, without the approach of dental caries; and in every instance after the removal of these teeth, the patient experienced distinct and marked improvement. This is a matter of extreme importance, for if the teeth may become involved as a result of the systemic rheumatism, as well as be an important causative factor, it will throw an entirely new light upon our responsibility in the care of arthritic cases. But this is so important a matter that I will make it a separate study in the next chapter.

SUMMARY AND CONCLUSIONS.

Characteristic localized structural changes develop in the supporting structures of teeth when the latter carry infection within their structures. These changes are, however, determined chiefly by the host and are an expression of the reacting characteristics of the host rather than an expression of the invading bacterium.

CHAPTER XL.

DENTAL INVOLVEMENTS CAUSED BY ARTHRITIS.

PROBLEM: Can arthritic infections of the body attack and devitalize the teeth?

EXPERIMENTAL AND DISCUSSION.

It has been presumed that the teeth are only subject to the diseases which may be directly caused from the entering in and around them of infection. Some years ago I noted in my records that all the bones of patients having arthritis of a certain type tended to be more dense than normal, while other types of arthritis tended to have little condensation, and in some instances definite reduction in the calcification. By studying the maxillæ in mandibles of these patients we have found that the medullary spaces were very much smaller and the trabeculæ formed a very much larger percentage of the body of the cancellous bone in patients with arthritis. It often took the form that resembled a quite uniform condensing osteitis throughout the entire mandible or maxilla.

One of these cases I have been studying for twenty-five years. In 1901 I roentgenographed her teeth and found that a filling in an upper right bicuspid, that had been put in years previously, did not extend to the apex, and proceeded thoroughly to sterilize and correctly to root fill it, for the teaching of that time was more confident than the teaching of today, that dental infections could be readily destroyed by any one of many forms of medication, if properly applied. As shown in my roentgenogram taken in 1901, there was definite apical absorption with a concentric arrangement of the trabeculæ about the apex, which I now take to indicate a series of exacerbations and reactions with condensation on a part of the inflammatory process. After this tooth was, as I suppcsed, perfectly sterilized and root-filled, I had what I probably showed, as many others are doing today, what I supposed to be evidence of my remarkable skill in sterilizing this tooth and making it safe for this patient; for, as shown in B of Figure 225, the apical area of absorption filled in, and from this indisputable evidence the infection had been all destroyed, which fact was also

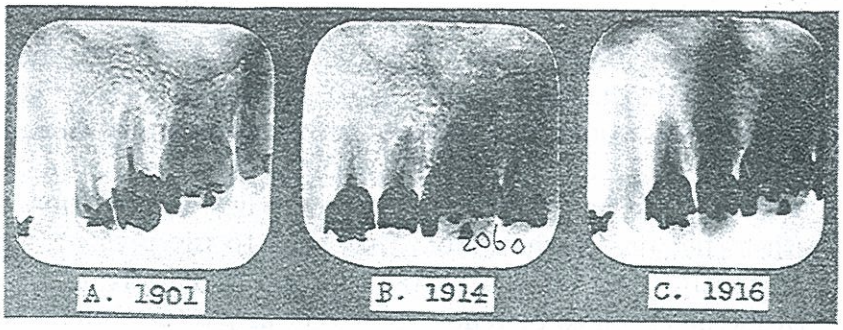


FIGURE 225. PROGRESSIVE DEVELOPMENT OF RADIOPACITY OF SECOND BICUSPID OF PATIENT WITH DEFORMING ARTHRITIS. A, IN YEAR 1901; B, 1914; C, 1916.

guaranteed by the symptom that the tooth was not in the least sore, and comfort endorsed the guarantee. But at the time I did this, this patient already had deforming arthritis following a severe attack of rheumatism, which had been so severe that her hands were already deformed and becoming rigid. Her ankles were also slightly involved. During the years from 1901 to 1916 I saw her occasionally, made dental repairs, and, as my researches progressed, I finally became very much alarmed and conscience stricken for fear the fact, that she was getting progressively and seriously worse, might be due in some part to my mistaken interpretation of the assurances of the success of my operations. I, accordingly, sent for her, at which time she was so nearly immobile that she practically had to be carried to the office. With the removal of these two teeth, with the condition as shown in Figure 225-C, she made a very definite and marked improvement.

But at the time of their removal I took great care to study her case in further detail. I undertook to remove the teeth without the possibility of the mouth infection's contaminating the roots, which was accomplished by using the actual electric cautery with which I seared the anesthetized tissue deep into the alveolar bone surrounding the necks of these teeth. Upon their extraction, I drilled into the apices and found both these bicuspids infected. (This matter of drilling into extracted teeth after sterilizing the surface, and culturing the chips has been done very many times in the last six years, and practically without exception I have found the teeth which I was testing to be infected.) But, in addition, I drilled into the bone a quarter of an inch beyond the apex and found the same strain of streptococcal infection in the bone. Three months later, under local anesthetic and actual cautery to

sterilize the surface, I again drilled into the periapical bone and found it still infected with this same strain. These findings, together with the fact that this patient who had been growing progressively worse, had now become progressively better, not only put me in a new attitude regarding her teeth, but put her in a state of such positive conviction regarding the relation of her teeth to her health that, from that time to the present, she has persistently urged that I extract all her remaining teeth. My attitude has been to be ready to extract any teeth that I thought might be doing her more harm than good, but since she could only put one hand to her mouth to remove a denture and would therefore, if she got much worse, be in a position where she could not handle artificial teeth, it seemed very desirable to retain such teeth as were definitely free from involvement and not subject to the possibility of contributing to her dental condition. Since that time, as stated above, six teeth, one after another, have become involved, (as evidenced by the symptoms which I will presently recite), and have one after another been extracted, after each of which extractions she has expressed a confidence that she felt definitely better. When asked how she knew, the reason she recently gave was that she had again become able to sew, a thing that had not been possible for years.

Just here I wish to introduce a warning: Exodontists and physicians who do not have the heart rending worries of making dentures comfortable and serviceable under conditions which are so nearly impossible as to very discouraging, but where the very nutrition of the patient demands a persistent effort, will be disposed to take the evidence just cited as justifying the extraction of all the teeth for this and similar patients. I wish to stress that we have come to the time when involved teeth can be so definitely differentiated from those that are not involved, or with sufficient limit of error, that we are not justified in condemning all of the teeth for fear they may be involved. I am seeing continually, patients who are suffering more from the inconvenience and difficulties of mastication and nourishment than they did from the lesions from which their physician or dentist had sought to give them relief.

In Figure 226 I have shown in a series, A to G, the six teeth that have been extracted since the above experience, one or two a year; and some interesting and important data have been accumulated regarding their conditions. In the preceding chapter, I have

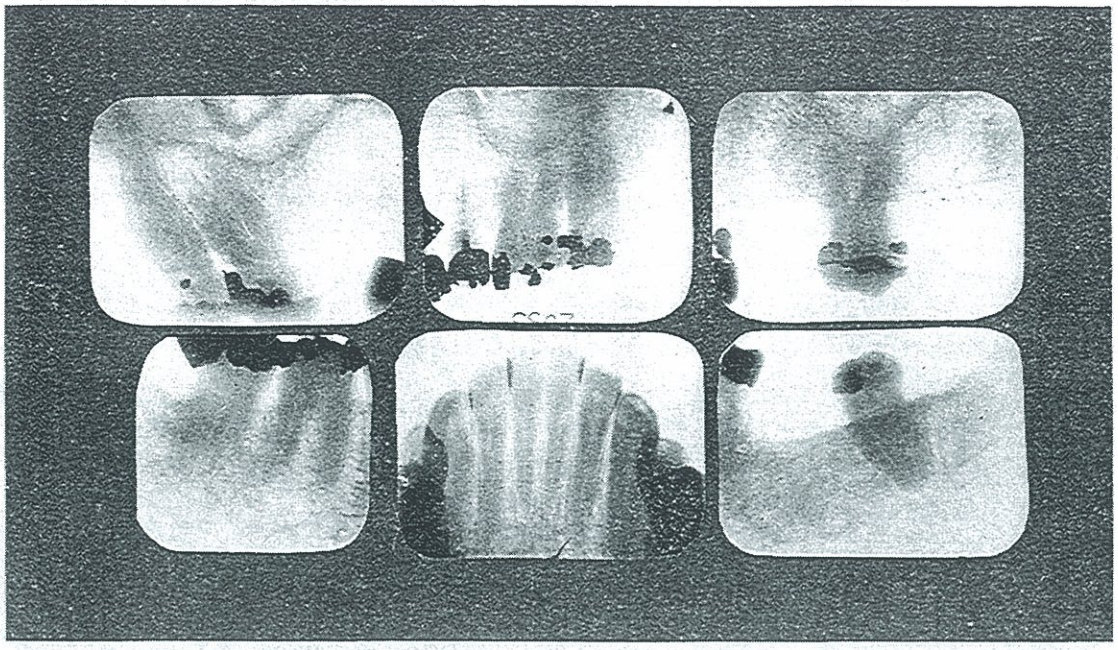


FIGURE 226. SIX TEETH WHICH BECAME NON-VITAL IN SUCCESSION IN THE MOUTH OF A PATIENT WITH DEFORMING ARTHRITIS.

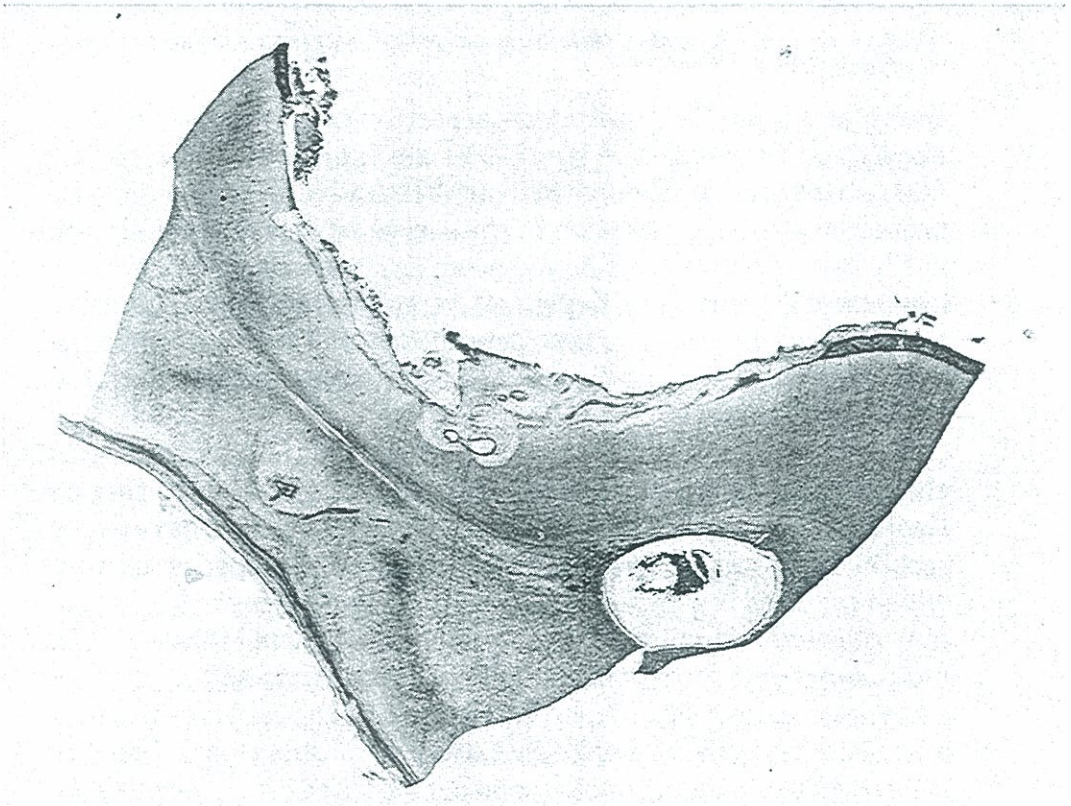


FIGURE 227. OSTEOCLASTIC ABSORPTION OF TOOTH STRUCTURES AND CALCIFICATION OF PULP IN A PATIENT WITH DEFORMING ARTHRITIS.

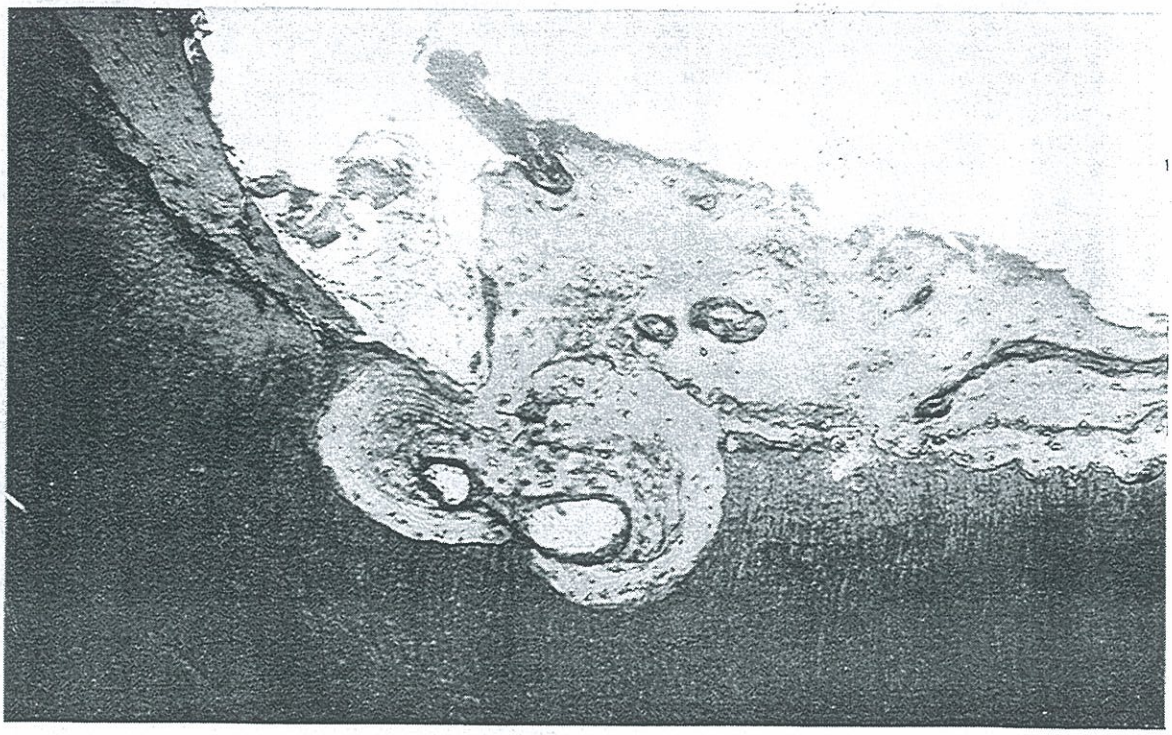


FIGURE 228. ABSORPTION OF CEMENTUM AND DENTIN AS PART OF ARTHRITIC DISEASE OF TOOTH SHOWN IN FIGURE 227.

shown in Figure 217 a histological section of the process of bone absorption, in which the giant cells are busy carrying away the bone structure. In Figures 220 and 221 I have shown some of the process of joint degeneration in the earliest stages of arthritis, and in Figures 218 and 219 I have shown illustrations of two types of rheumatic arthritis, one degenerative and the other proliferative, as evidenced by the marked depositions of the bones involved in Figure 218-B, C, and E, and the destruction and absorption of the head of femur in 219-B.

With these processes in mind, let us study the histological changes that have been taking place about the teeth of this patient as they have become involved. In Figure 227 we have a cross section of an upper left molar which had developed symptoms which made me suspicious that it was degenerating. The beginning of calcification of the pulp of one of the roots is shown. But more important for this immediate consideration is the process of absorption taking place upon the surface of the root, for it will be seen that an inflammatory irritation is in progress, which has destroyed the cementum of a considerable area and is penetrating far into the dentin. Figure 228 shows a larger view of this process, and it will be seen that this structure is highly vascularized and is

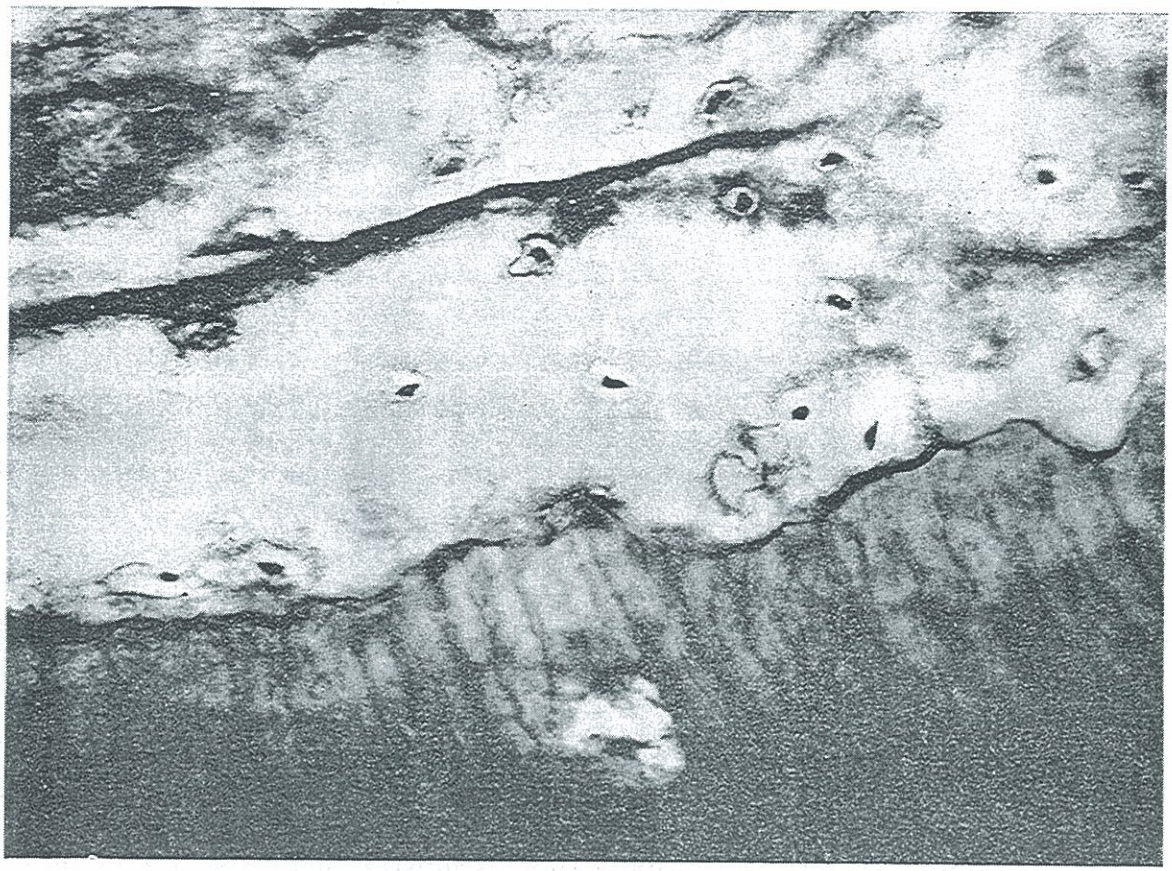


FIGURE 229. OSTEOCLASTIC ACTIVITY, HIGH POWER, OF FIGURE 228.

abundantly filled with a special type of cells and that it is burrowing deeply into the dentin. A still higher magnification of this condition is shown in Figure 229, in which it will be seen that these giant cells are very abundant. Some are in close contact with the dentin; others are migrating. We have in this process a reaction very similar to that taking place in degenerative arthritis of joints. This is distinctly shown in Figure 230, which is a histological section of an acute inflammatory process produced in the joint of a rabbit by the inoculation of a strain producing arthritis; and it will be noted that the process is almost identical with that we have taking place about this tooth.

If we would refer again to Figure 227, we will note the beginning of decalcification of this pulp. Figure 231 shows a higher magnification of this, and it will be noted that the zones of calcification tend to develop around blood vessels and in the odontoblastic layer. The pulp tissue has largely lost its original structure. Fibrous bands are forming beneath the odontoblastic layer and around the blood vessels, and these in turn are becoming calcified. In other illustrations, we have shown lamination of pulp depositions by the successive layers becoming calcified. This process may go

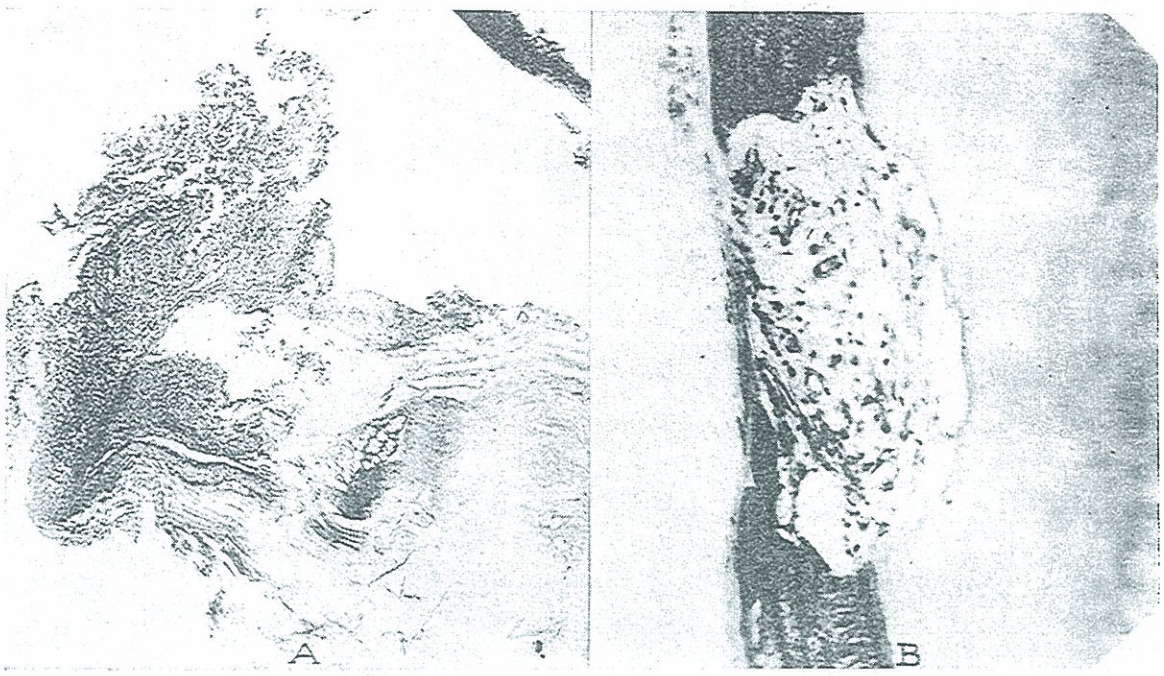


FIGURE 230. OSTEOCLASTIC REACTION PRODUCED BY RABBIT: A, IN AN ARTHRITIC JOINT; B, IN AN IMPLANTED AND ENCYSTED TOOTH.

on until the pulp has been very largely, or practically completely, obliterated by calcification. This is illustrated by one of the teeth extracted from this patient, a cross section of the root of which is shown in Figure 232. When the roots were cut from this tooth at the crown, it was found that not only were both roots completely calcified, but the entire coronale part of the pulp chamber was filled with a closely fitting casting. One huge pulp stone had apparently come to fill the entire pulp chamber. By referring to the roentgenogram of this tooth, shown in Figure 233, it will be noted that there was no evidence of root canals or of pulp chamber. This latter fact should be considered very important, as will be shown in the diagnosis of this condition.

A very important factor regarding this tooth (the upper right first molar) was the following: that notwithstanding this extreme and apparently complete calcification of the pulp, the tooth was not only hypersensitive to hot and cold, but was sensitive to irritation of the exposed dentin to instrumentation. The patient complained that she would be awakened in the night by the pain in this tooth resulting from her mouth's opening when she was asleep, and the cold air chilling the tooth would produce so violent

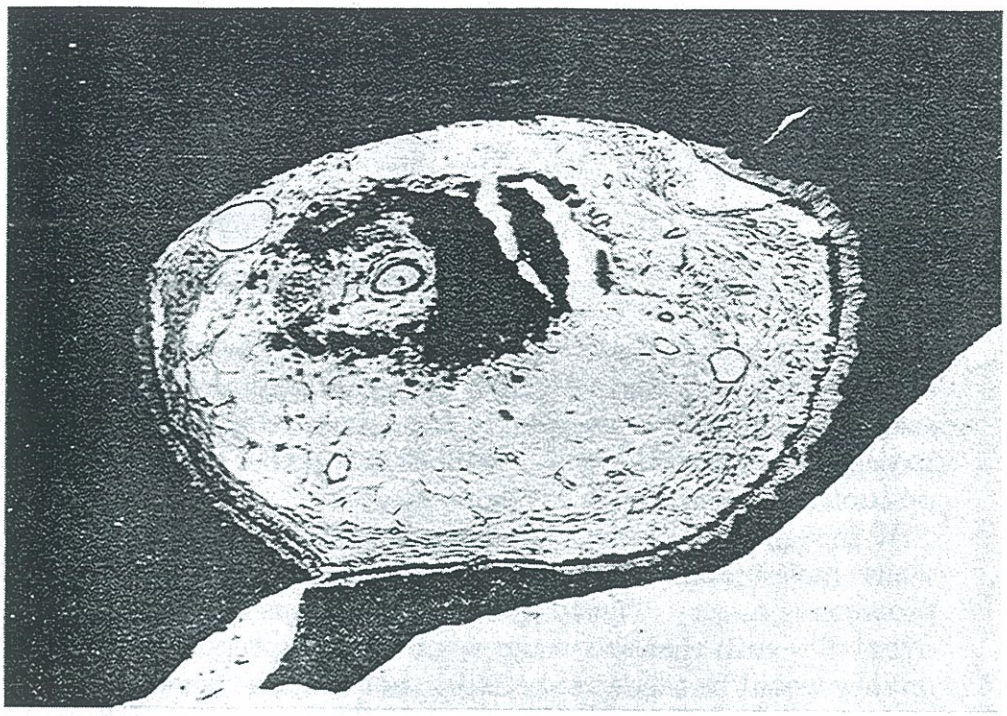


FIGURE 231. CALCIFICATIONS IN THE PULP OF TOOTH SHOWN IN FIGURE 227.

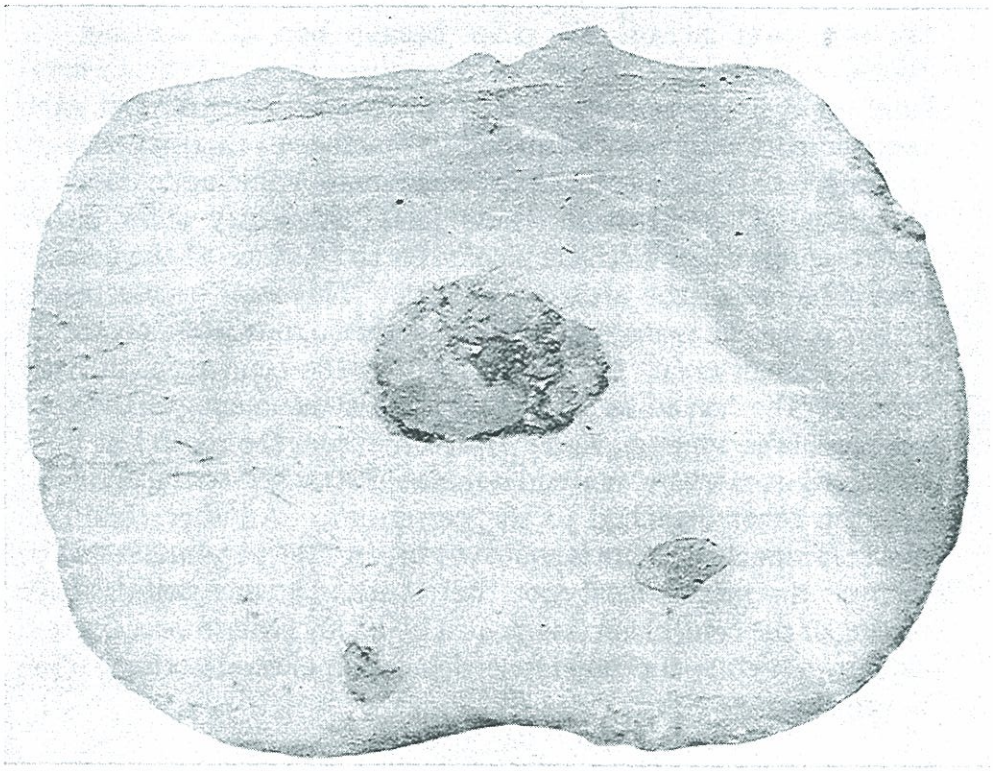


FIGURE 232. CROSS-SECTION OF A DECALCIFIED PULP FROM A PATIENT WITH ARTHRITIS.

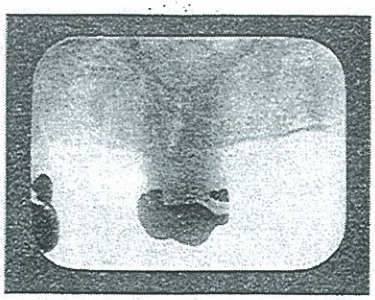


FIGURE 233. ROENTGENOGRAPHIC APPEARANCE OF TOOTH WITH COMPLETELY DECALCIFIED PULP, SHOWN IN FIGURE 232.

a toothache that it would waken her. After her mouth had been closed a sufficient length of time, the tooth would become warm and the pain would cease, all this to be repeated if she continued to sleep in a cold room, for she could lie only on her back, in which position the mouth tends so readily to open.

With regard to the matter of diagnosing these teeth, those teeth which have become involved have passed through the following progressive history. There would be symptoms of tenderness or irritability such that she would want to make pressure on them, or they would be tender to pressure, not acute as develops from pericementitis from an infected pulp. This stage was followed by one of hypersensitiveness to heat and cold. In two of the teeth where she did not heed these symptoms promptly enough, the two lower incisors, the pulps became non-vital and non-responsive to thermal change. Two or three times a year we carefully go over the remaining teeth of this patient and test each tooth in succession for normality to reaction to thermal change, to history of tenderness and the roentgenographic appearance of the pulp. On extraction, these teeth frequently show either macroscopically or microscopically on the surface of the cementum evidence of the arthritic process. This may be illustrated in low power or macroscopically by either a roughened condition of the cementum or the attachment to the cementum of little fibres by the frayed ends of the frayed attachments of the supporting fibres which have not torn loose from the tooth but have been broken midway, one end remaining attached to the alveolus, and the other attached to the cementum. Another condition which frequently occurs is shown in Figure 234, in which it will be seen on the mesiobuccal root that there is at one point a deep pitting of the cementum and dentin by an absorption process, and close by a nodule of proliferative deposition of osteoid tissue upon the cementum.

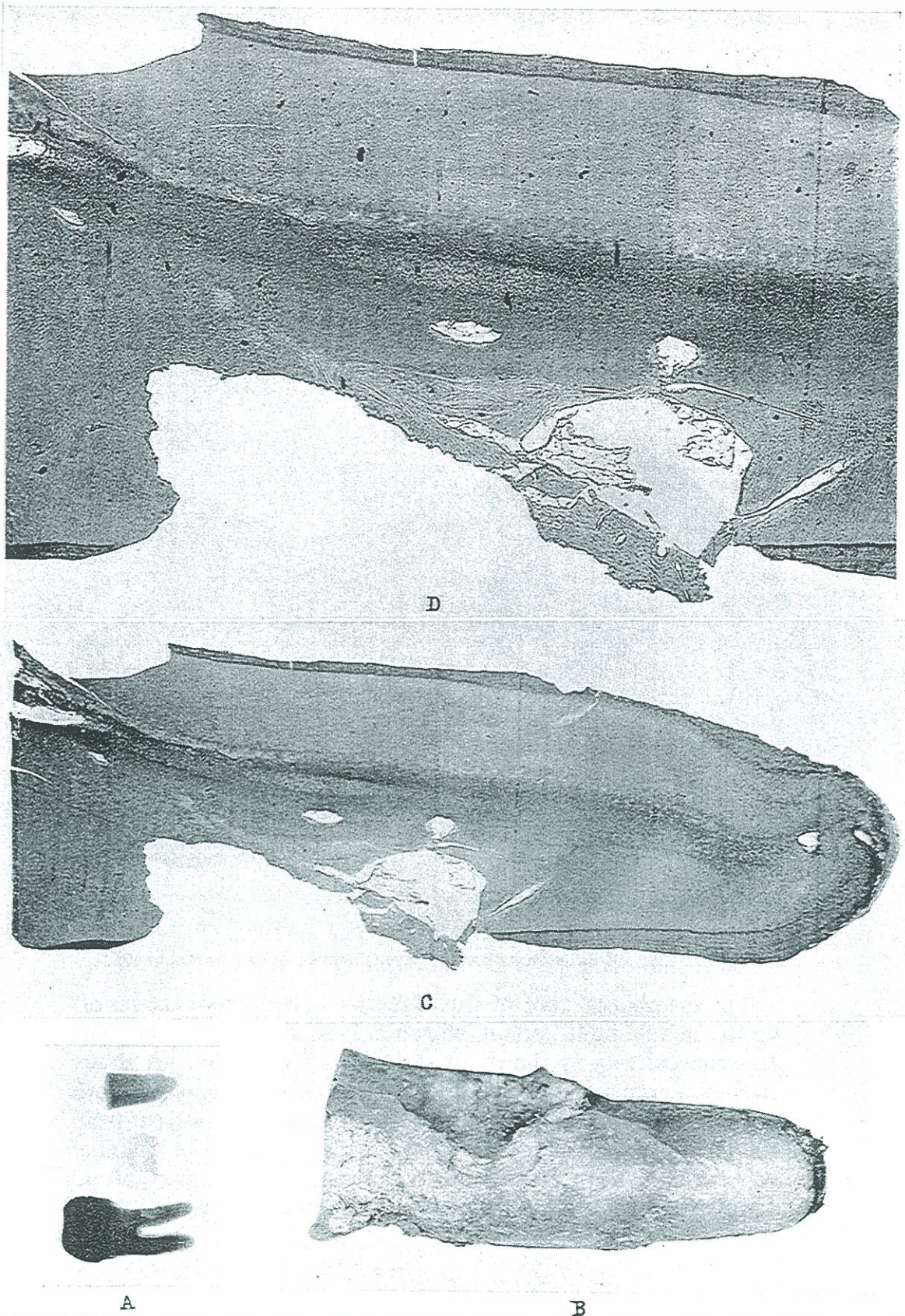


FIGURE 234. ARTHRITIC CHANGES IN EXTERNAL SURFACES OF TOOTH WITH CALCIFIED PULP FROM ARTHRITIC PATIENT.

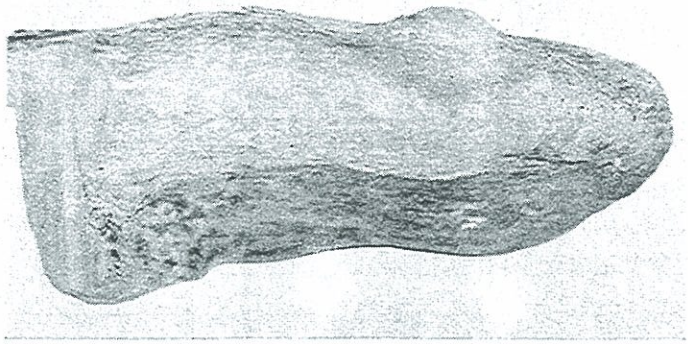


FIGURE 235. ARTHRITIC HYPERTROPHIC NODULE ON ROOT.

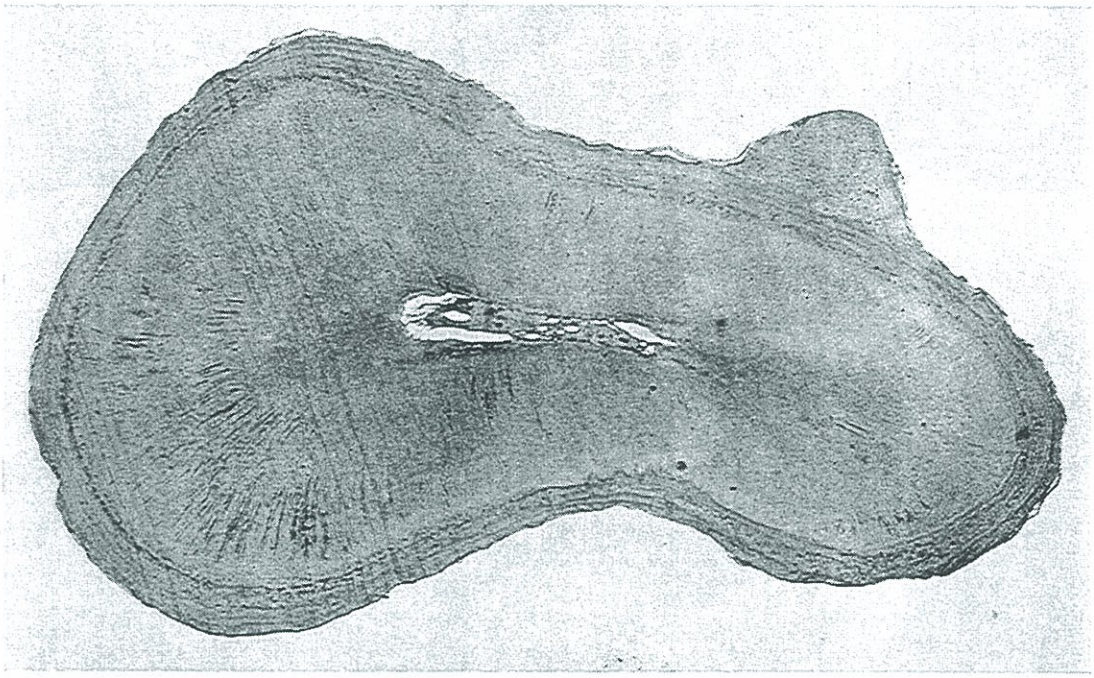


FIGURE 236. CROSS-SECTION OF HYPERTROPHIC NODULE, SHOWN IN FIGURE 235.

The distobuccal root of this same tooth had even a larger arthritic nodule built upon it, shown in Figures 235 and 236. The mesiobuccal root is shown in the cut in Figure 234. A shows roentgenograms of the two buccal roots of the extracted tooth and separately of the palatal root and of a small section cut from the palatal root to illustrate how completely the pulp chamber was calcified. B shows this deeply burrowed pit with the built up nodule of osteoid tissue. C and D show these two structures in

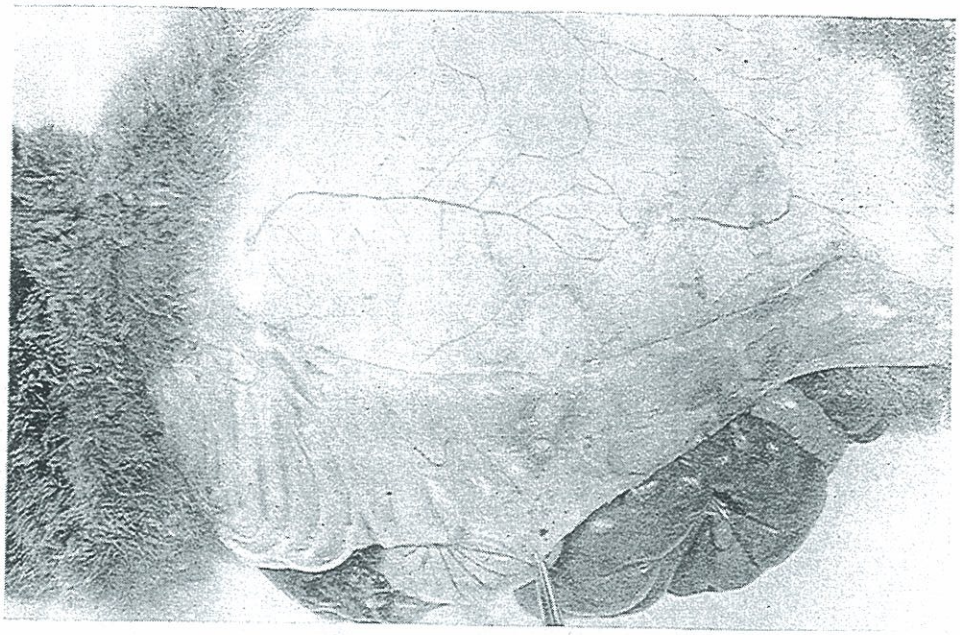


FIGURE 237. SKIN LESION OF RABBIT WHICH LOST 28 PER CENT IN WEIGHT IN TWENTY-TWO DAYS, FROM IMPLANTATION OF CALCIFIED ROOT FROM ARTHRITIC PATIENT.

cross section and higher magnifications, and it is of interest to note that the nodule is bridged over an open space, or, as it were, a cavern in the dentin with two other caverns shown deeper in the dentin.

When we remember that this tooth was not only responsive to thermal changes but was really hypersensitive and painful, showing a clearly exalted vital response, we would naturally not look upon it as being infected structure. The palatal root, therefore, when it was cut from the freshly extracted tooth, was immediately planted beneath the skin of a rabbit to determine whether it was an infected structure capable of doing the animal injury. A section of the tooth was also cultured. The rabbit shown in Figure 237, under the skin of which was planted the palatal root of the tooth we have been reviewing, died in twenty-two days, having lost 295 grams, or 28 per cent of its weight, or nearly 1½ per cent per day.

Returning to the discussion and study of the pathology of the pulp, some very interesting features had developed. As stated previously, not only was the pulp tissue of the roots entirely calcified, but also the bulbous portion. High power magnifications of this pulp tissue are shown in Figure 238. In A will be seen channels through which the blood vessels passed, and around which the calcifications developed. In B will be seen what appears very

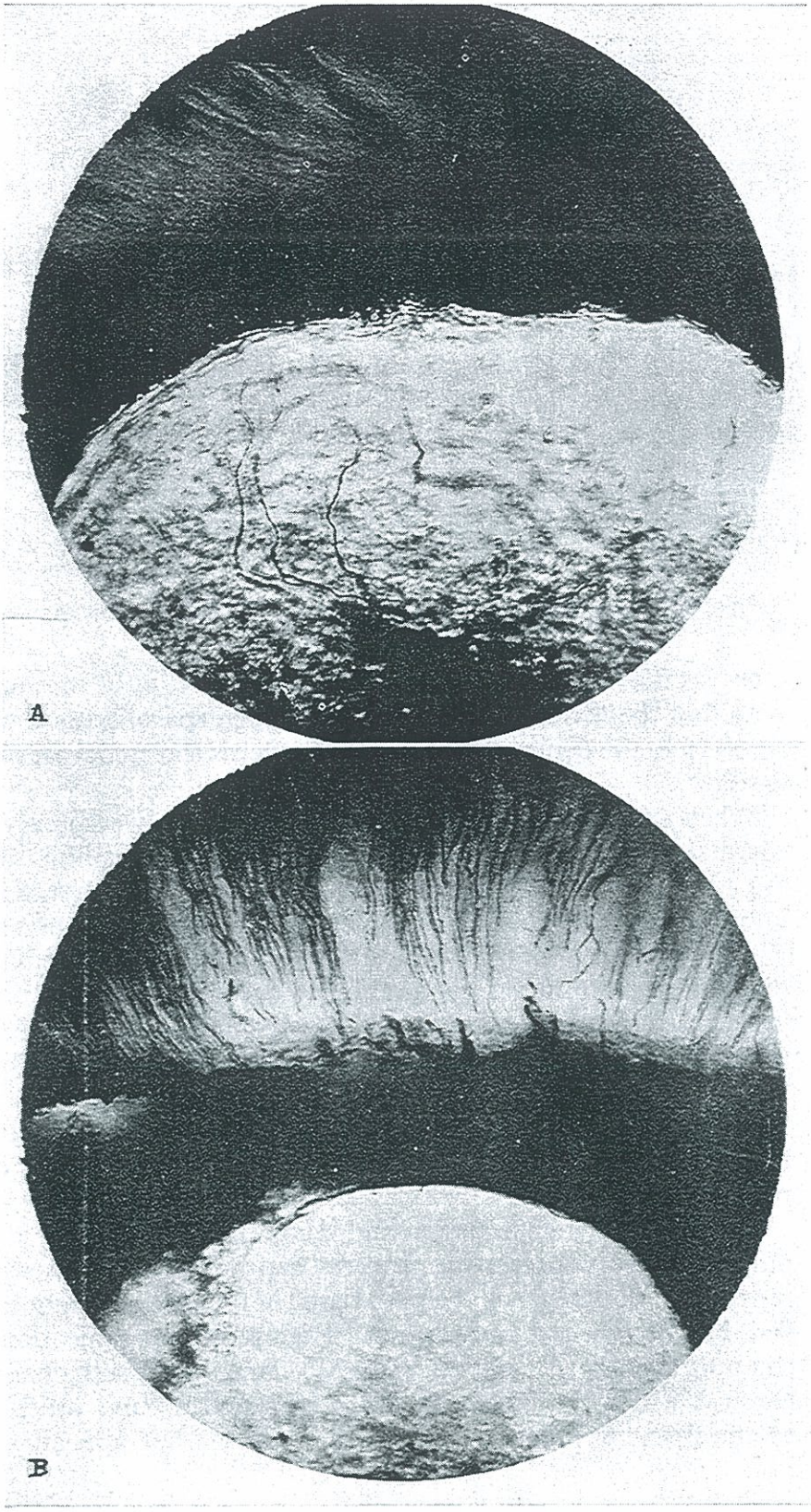


FIGURE 238. HIGH MAGNIFICATIONS OF SECTIONS OF CALCIFIED PULP. NOTE DENTIN-LIKE STRUCTURE IN B.

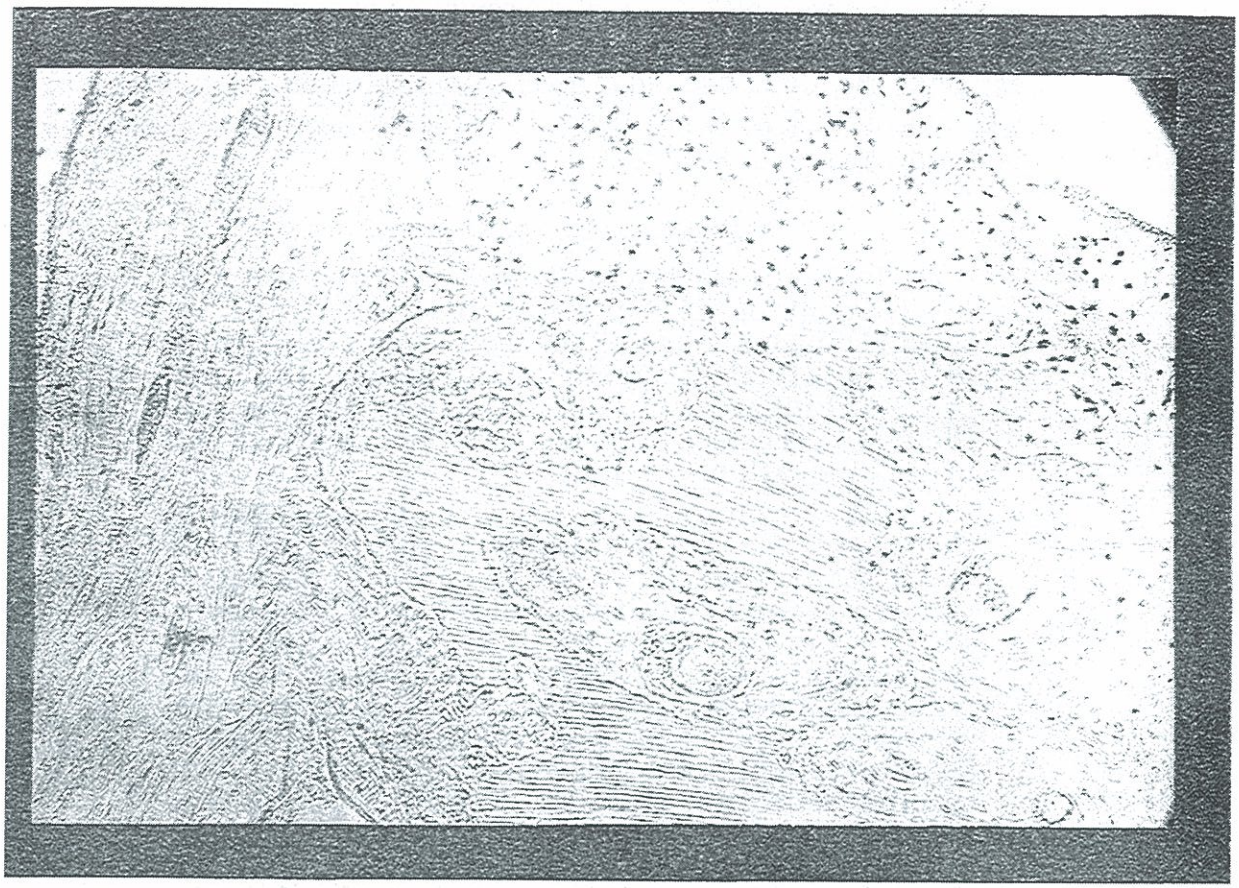


FIGURE 239. SECTION OF ALVEOLAR BONE FUSED INTO A ROOT FOLLOWING AN INFLAMMATORY REACTION.

similar to dental tubuli. But these are not in dentin; they are in this osteoid structure radiating from one of these blood vessel chambers which is shown in the lower part of the field. They do not, in this view show an intercommunicating system of connecting channels, each appearing to be dependent throughout its course. We have frequently found these in calcified pulps, and it is not impossible that they are in some way related to, either in origin or in structural type, the dentinal fibres of the odontoblasts.

It frequently occurs that this degenerative process subsides, or there is a reversal so that an absorption process is transferred into a proliferative one, and this same tissue, which up to the time of the change in systemic conditions was engaged in the tearing down of osseous and dental structures, proceeds to fill up the chambers it has burrowed out with a new structure. Of course, it cannot reconstruct dentin or cementum, not having either odontoblasts or cementoblasts; but it does have osteoblasts. It, accordingly, builds an osteoid structure, sometimes with an haversian system very closely resembling true bone. This con-

stitutes what we have discussed as a condition of ankylosis. This is typically illustrated in Figure 239, in which instance, when I extracted the tooth, I found it necessary to chisel off every little piece, there being no clearly defined zone of cleavage between the tooth structure and the alveolus.

SUMMARY AND CONCLUSIONS.

(1) It will be seen from these data that a systemic involvement of multiple arthritis may, while attacking various joints of the body, also attack those of the joints of the teeth; and, further, that this process of inflammation with degenerative and proliferative processes may cause the involvement and ultimate death of the pulp.

(2) The involvement of these teeth as a result of the progressive systemic arthritis may in turn, and doubtless frequently, if not generally, does aggravate the general condition, for the tooth structure, when it becomes infected, is even less capable of vascularization and therefore less amenable to the processes of defense, than is bone. This stresses the very great importance that, individuals having deforming arthritis, shall have most careful dental inspection and care, and also, since it is one of the most horrible of living deaths, every effort should be made to prevent the beginning of that process; and since the evidence is so overwhelmingly that the initial infection frequently, if not generally, comes from the teeth, helpless humanity deserves pity until the powers that be shall make a worthy effort to find the means that will prevent this needless catastrophe in so many lives.

CHAPTER XLI.

VARIATIONS IN THE DEFENSIVE FACTORS OF THE BLOOD.

PROBLEM: Is there a difference in the defensive factors of the blood of susceptible and non-susceptible individuals to systemic involvements from dental infections?

In the preceding chapters, the data secured from the researches seemed to demonstrate the following:

In Chapter 3 we found that the same dental infection expresses itself quite differently, locally, in the supporting structures about the teeth in different individuals.

In Chapter 4 there is a very marked variation in the susceptibility to systemic involvement of different individuals, which susceptibility tends to be a family characteristic.

In Chapter 5 we found that these characteristics of both the local and systemic expressions are definitely related each to the other.

In Chapter 20 on Blood Calcium we found a definite relationship between the calcium content of the blood in different types of individuals, which had been grouped in accordance both with their type of local oral pathology and systemic susceptibility.

In various other chapters we found characterizations and relationships which were distinct, as, for example, the relationship to dental caries, periodontoclasia, rarefying and condensing osteitis, etc., etc.

In Chapter 38 the evidence seemed to demonstrate that the so-called dental granuloma is a physiologically acting tissue and not necessarily a degenerative type of tissue, though it may become such with a loss of function of that tissue; and that tissue, when taken from an individual with high defense, as judged from the fact that he was not having any apparent systemic expression from involved dental infections, would, when placed on or in infected culture media, show a marked inhibitive power on bacterial growth as well as produce a bacteriolysis.

In Chapter 20 we found that when an infected tooth is placed

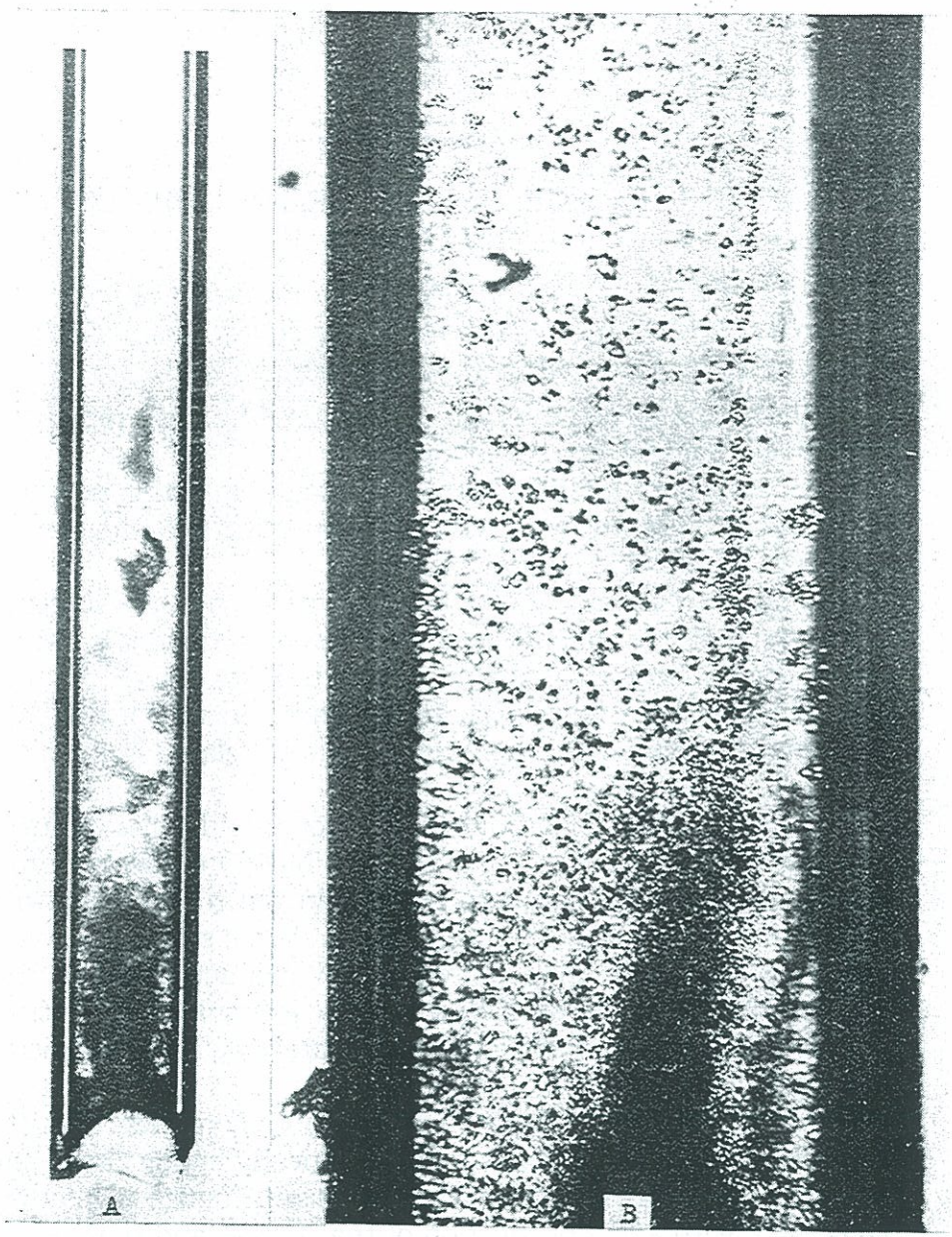


FIGURE 240. THE MIGRATION OF LEUCOCYTES INTO A GLASS TUBE, A CHEMOTACTIC REACTION WITH TOXIN.

beneath the skin of a rabbit, either the rabbit builds such a defensive membrane (in which case it is not seriously injured, or at least not promptly so), or else the rabbit's defense is rapidly lowered and it dies in a few days; and in that chapter as in preceding chapters, we found that the placing of such a tooth under the rabbit's skin produced changes in the rabbit's blood, particularly in the blood calcium, and that its prostration was largely in direct proportion to depression of the ionic calcium and the production of a pathologically combined calcium.

In Chapter 20 we found that the placing of an infected tooth in the blood serum of a patient or animal tended to reduce the ionic calcium of the serum and produce a pathologically combined calcium, and that this condition was apparently identical, whether it developed *in vitro* or *in vivo*.

If, then, the dental infection acts directly upon the defensive forces of the circulating blood, it should be possible to measure and determine these, or at least it would be of very great advantage if this can be done. To determine this, we have made the following special studies. For some time we have been studying the action of the leucocytes in the presence of various types of irritants and chemicals. It is most significant, as has been shown by others, that when a capillary glass tube containing bacteria, dead or alive, is placed beneath the skin of a rabbit, the leucocytes tend to be attracted by chemotaxis to these bacterial products and migrate rather rapidly into the glass tube. Such a condition is shown in Figure 240. In order to determine the depressing effect on the quality of chemotaxis, I have placed tubes containing cultures grown from dental infections beneath the skins of normal rabbits and have noted the distance into the tubes that the leucocytes would travel in a given time. It was found that the leucocytes migrated in large numbers to a considerable distance within the tube. One end of the tube was sealed, the open end filled with the infected culture media being in direct contact with the subcutaneous tissue as the end of the tube was slipped under the skin. When a similar tube was placed under the skin of a rabbit, into which a tooth had been planted a few days previously and for which the rabbit had sufficient defense to build an encapsulation without the production of pus or evidence of other local irritation, it was found

that the tube placed not within, but in the vicinity of this cyst, had a very much less profuse migration of the leucocytes than did the normal rabbit. When we placed a tube under the skin of a rabbit which was not showing such good reaction to the tooth, for pus was developing and the animal was rapidly losing in weight, the tooth having been planted several days previously, it was found that the organisms did not penetrate so far nor so rapidly as in the normal tissue.

When we undertake to relate these data—namely, that the defense of the rabbits is not only measurable in quantitative terms by a study of the chemistry of the blood, but in the physical expressions of the leucocytes themselves—we find what seems to be a very direct placing of the responsibility for a large part of the mechanism of defense upon the leucocytes. In order to study this more exactly, I have made the following important experiments: The blood has been taken from normal animals and humans and its power to kill streptococci taken from teeth determined both with regard to quantity of organisms and the time necessary to destroy them, by placing the live organisms of a known number in the freshly drawn blood, with or without defibrination, for different periods of time, varying from one minute to sixty minutes; and since the number of live organisms was known with quite close approximation to exactness by counting and carefully measured diminutions, it became possible to test not only the capacity of the blood for reacting in the devitalizing of the live organisms, but to establish the rapidity of this process. It has been most striking and unexpected to find that the blood of normal healthy animals and normal individuals with a high defense will not only kill these organisms in very large numbers, but that it will do so in one minute's time, for the difference between the effect of leaving the organisms one hour or ten minutes leaves so little advantage in favor of the longer time that nearly the maximum devitalizing effect has occurred in ten minutes, and, indeed, in many bloods this process is almost as efficient in one minute as in one hour. Contrary to our expectation and the current teaching regarding the mechanisms of defense, which have provided that the leucocytes engulf and phagocyte the bacteria, we have found that in this devitalizing process very few of the organisms, or at least a very small percentage, have been engulfed; by far the great majority have been devitalized; and if the blood stains are not examined within a few minutes, the

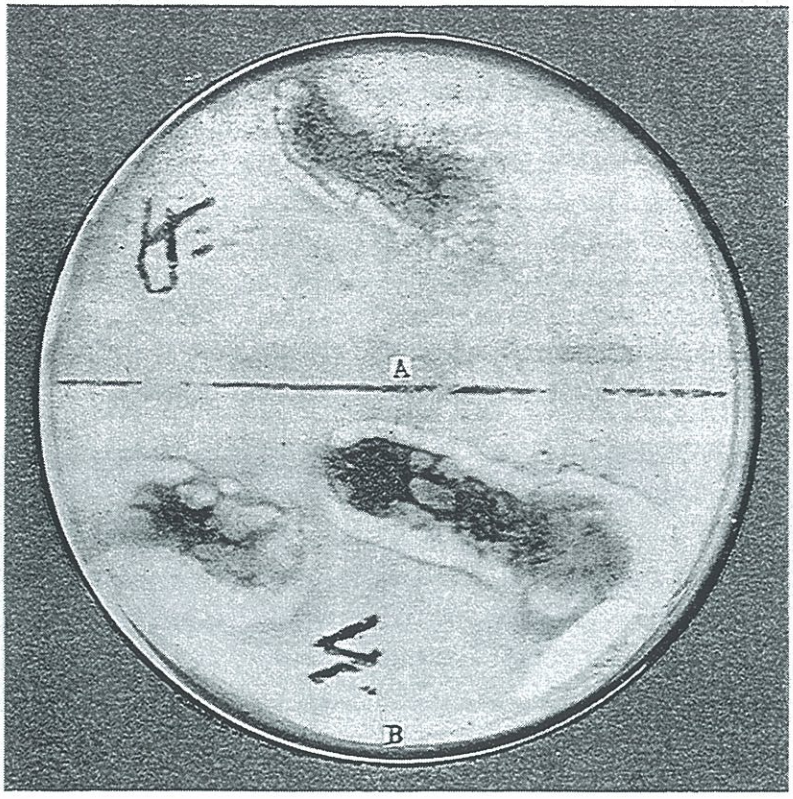


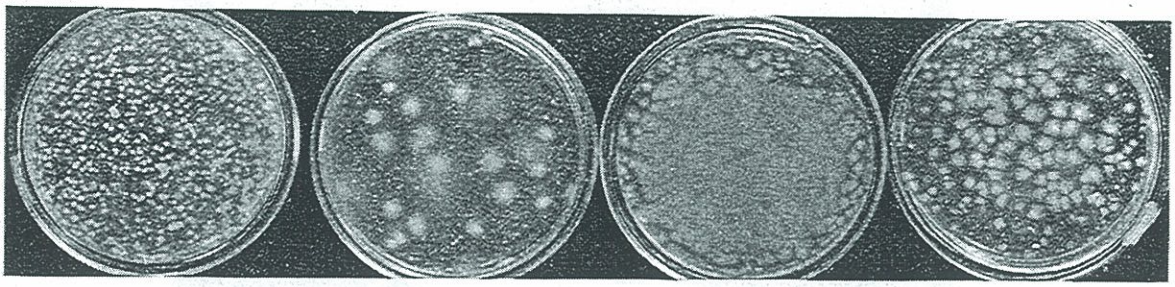
FIGURE 241. A COMPARISON OF A DROP OF BLOOD FROM A DEFECTIVE PATIENT—A, WITH A NORMAL PATIENT—B. NOTE THE CLEAR ZONE IN B, INHIBITING BACTERIAL GROWTH.

organisms will not only be devitalized, but will be digested by special enzymes provided by the blood.

Before taking up a detailed study of the relation of time and the different bloods in this devitalizing process, I wish to review experiments made by placing drops of various bloods on infected agar plates. Figure 241-A shows one drop of blood taken from a patient with a chronically low defense to streptococcal infection, suffering from xerostomia and rheumatism, and two drops of my blood in B. It will be noted that the organisms not only do not grow in or under the drops of my blood, but there is a zone for a considerable distance around my blood where this inhibition has been complete; whereas, in this patient's blood the zone is very diffuse and but slightly marked, and the organisms are growing under and over the blood. There is clearly a very great difference in the bactericidal property of these two individuals.

Important new data have been added to the available knowledge regarding the defensive factors of the blood by Sir Almroth

Wright. In the bibliography I have given references to several of his contributions. His original work on the determination of the opsonic index of the leucocytes started a new interest in these structures. During the war he made important observations regarding the defensive factors which are localized in individual wounds, such, for example, as the finding, that some wounds of a given patient had not only rid themselves of infection, but would destroy organisms that were abundant in another wound of the same patient when the dressing from the latter wound was placed on the healing wound, thus showing that the defensive factor was in part, at least, a local tissue reaction quality.



A B C D

FIGURE 242. STUDIES OF BACTERICIDAL PROPERTY OF BLOOD, ONE MINUTE EXPOSURE.

In order to establish more exactly this quality of defense of different groups, I have made an extended series of platings, in which I have used the blood of the patients under study, in comparison with normal controls, to establish, if possible, the nature of the variations. In Figure 242 will be seen four Petri dishes. A is a control and contains approximately five hundred organisms placed in the agar of the Petri dish. B shows the result of taking a cubic centimeter of blood from a normal rabbit and placing these living organisms in this normal rabbit's blood for one minute. The infected blood was then placed in the agar, and it will be noted that the five hundred organisms were reduced to about fifty. A similar quantity of the counted culture was placed in a similar quantity of blood of a rabbit that had been infected by placing a tooth under its skin, shown in C. It will be noted that a large number of colonies grew out, that the infected rabbit was not able to devitalize as many of the bacteria in one minute's time as did the normal rabbit. D shows the effect of taking some of the blood from a patient whose defense has been lowered and who was suffering from rheumatic symptoms. It will be noted that while he killed more of the organisms than did

the infected rabbit, he did not kill nearly so many as did the normal rabbit.

When, however, we compare the effect of using a large number of organisms instead of five hundred, even though the organisms are exposed to the blood for sixty minutes, we find a very different reaction. The result of this is shown in Figure 243. The controls, shown in A-1 and A-2, show respectively five thousand and fifty thousand organisms in the agar plates. The normal rabbit was able to kill nearly all of the five thousand and a very large

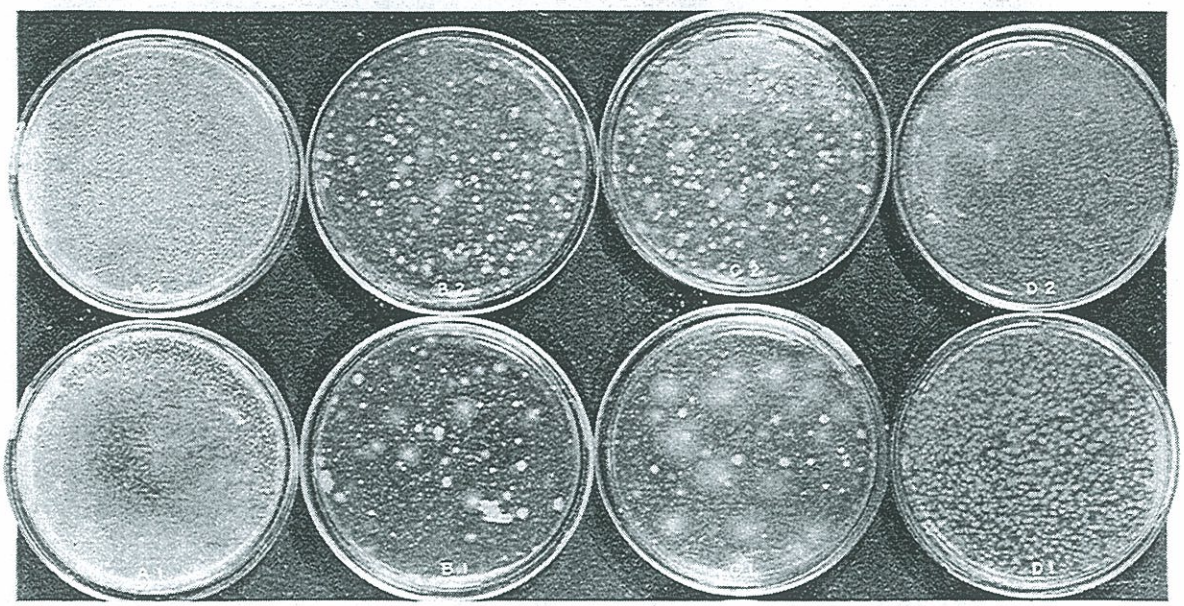


FIGURE 243. COMPARISON OF BACTERICIDAL PROPERTY OF BLOOD OF A NORMAL AND AN INFECTED RABBIT.

percentage of the fifty thousand, as shown in B-1 and B-2. The infected rabbit did not do so well as the normal rabbit, but showed a good reacting power. (See C-1 and C-2.) The rheumatic patient, however, did not do nearly as well as either the normal or the infected rabbit, shown in D-1 and D-2.

Another illustration of the difference in the bactericidal property of the blood of a patient with recurring attacks of rheumatic disturbances is shown in Figure 244, which gives two different dilutions of organisms in A, one marked 8x and the other 65x, where x is supposed to be a number approximately a thousand. When this quantity, approximately eight thousand, was placed in one cubic centimeter of my blood for ten minutes, the reduction in growth was reduced from that shown in A to that shown in B, the reduction being very great in both the eight thousand and the

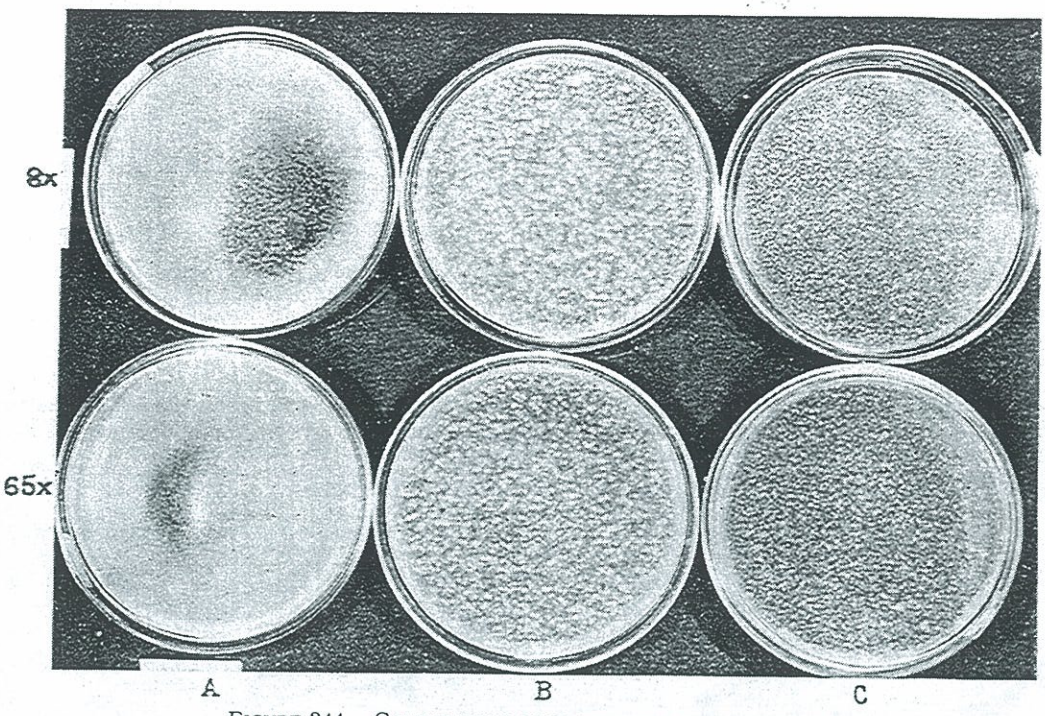


FIGURE 244. COMPARISONS OF BLOODS OF TWO INDIVIDUALS.

sixty-five thousand quantities of organisms. When these same quantities of the living organisms were placed in one cubic centimeter of the blood of this rheumatic patient for ten minutes, there was a reduction in the total number of organisms, as shown in C, but the reduction was not nearly so great as it was in the case of my blood.

At this point it would be well, perhaps, for me to make an explanation of the appearance of the Petri dishes. Bacterial cells, like plants, cannot grow normally if in too crowded a location. Consequently, in heavily inoculated Petri dishes the cultures are very small, each colony reserving about it an elbow room, so to speak; or rather, each takes from the soil nutrient material and gives off toxic material. Therefore the colonies tend to keep their individuality as units rather than coalescing; and the fewer organisms there are to grow in the space, the larger the colonies grow, just as a single tree will grow large with wide spreading branches, while crowded trees do not do this.

In Figure 241, I showed the difference in the bactericidal power of the blood of a rheumatic patient as compared with my own as normal, and called attention to the fact, that there was a zone of inhibition for a considerable distance around the blood on the

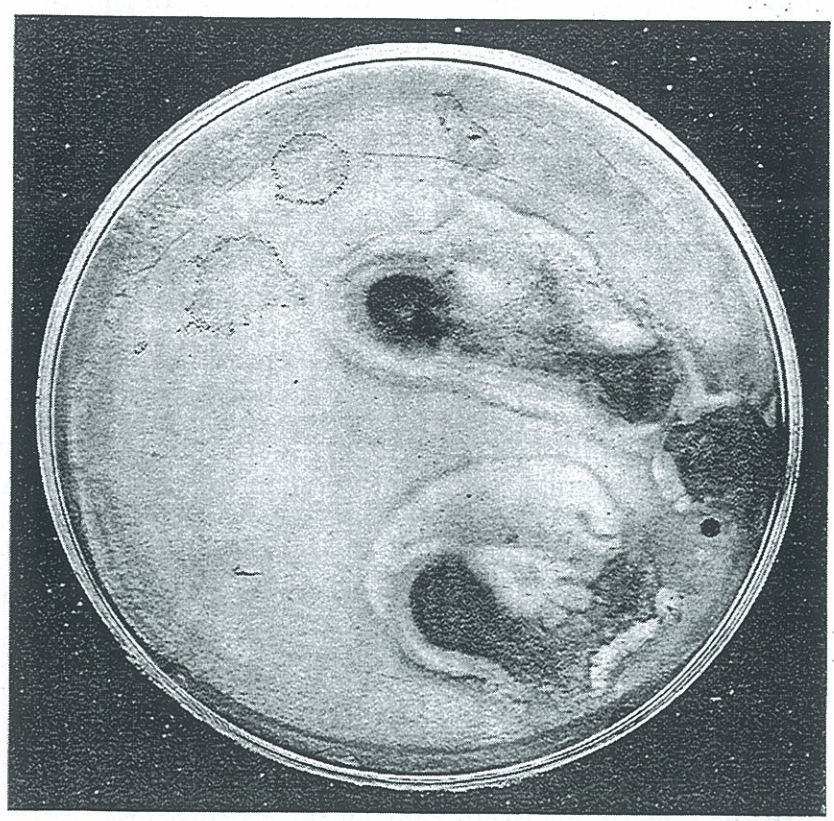


FIGURE 245. A BLOOD WITH A HIGH DEFENSE FROM A PATIENT RECOVERED FROM SYSTEMIC INVOLVEMENT.

infected agar plate. When such a patient has had infected teeth removed, which were apparently very materially disturbing the defensive factors, there is a marked improvement in this defensive quality of the blood, as shown by these various tests. Figure 245 shows such a case. This patient has returned to a vigorous normal health after having been ill for three years with symptoms variously interpreted as heart, digestive, and nervous system involvements. It will be seen here that his blood has now (three months after the removal of his infected teeth, during which time he has made a very rapid return to normal) become very highly defensive.

That infected teeth produce important changes in the blood can be shown in many ways. I have, in the preceding chapters, demonstrated their influence on the ionic calcium of the blood, the development of leucopenia, erythropenia, leucocytosis, etc.; and in Chapter 19, I illustrated the direct effect of the infection, whether injected or whether a tooth was planted beneath the

skin of a rabbit, in reducing the hemoglobin. In this connection let me refer particularly to the experiments in Chapter 20 on Chemical Changes in the Blood, in which I showed that the placing of an infected tooth in either the blood of a patient or in normal blood tended to produce changes directly in the blood chemistry.

In order to determine, if possible, whether the tooth toxins tend to produce an hemolysis, I have placed extracts of infected teeth with blood and have also made comparisons of the effect of placing droplets of the blood, so exposed, on infected Petri dishes for comparison with normal blood or the same blood before exposed to the infected tooth. This is very excellently demonstrated in the colored plate in Figure 246, which shows in A three drops of normal blood placed on an infected agar plate; B, a similarly infected plate on which have been placed four drops of a patient's blood who was suffering from nervous breakdown and neuritis. It will immediately be seen that the organisms have grown well on and over the blood of the suffering patient, whereas the normal individual has greatly inhibited the growth on the infected plates. In C we have two drops of the patient's blood placed on a similar plate, but before doing so the blood was exposed to broken chips of this patient's own infected tooth, with the remarkable result that all the erythrocytes, practically, have been hemolyzed and the coloring matter has disappeared almost entirely from the droplets and is in solution in the free moisture in the margins of the dish. All of this suggests, if it does not demonstrate, that these teeth contain substances which have a very marked influence on the blood of the patient.

Another important study has been to determine the nature of the response that is called forth in the blood by the tooth toxin as compared with the bacteria from the tooth. To determine this we have vaccinated the drawn blood from rabbits and patients with dead organisms, to determine to what extent the blood was able to respond to increased attacking power; for, as Wright has shown, the defensive elements of the blood cannot be estimated, or, at least, are not indicated by the primary response to a bacterial invasion that is not great enough to call forth the greatest activity. I have, accordingly, taken the blood and subjected it to dead organisms of the kind that the media would later be inoculated with, and, after holding this vaccinated blood, containing a given amount of dead organisms, for from

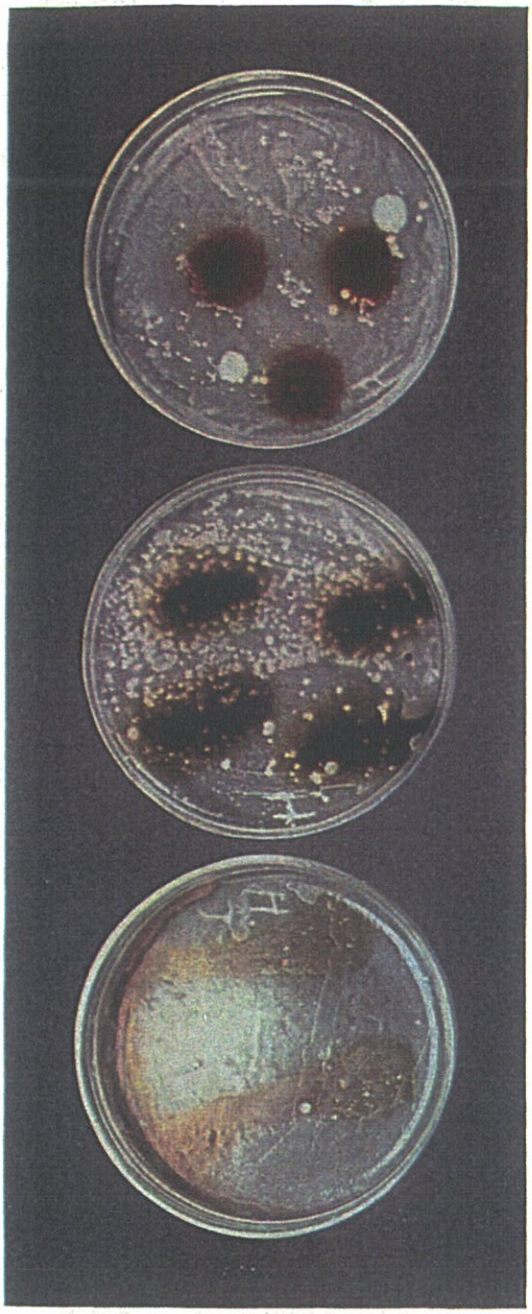
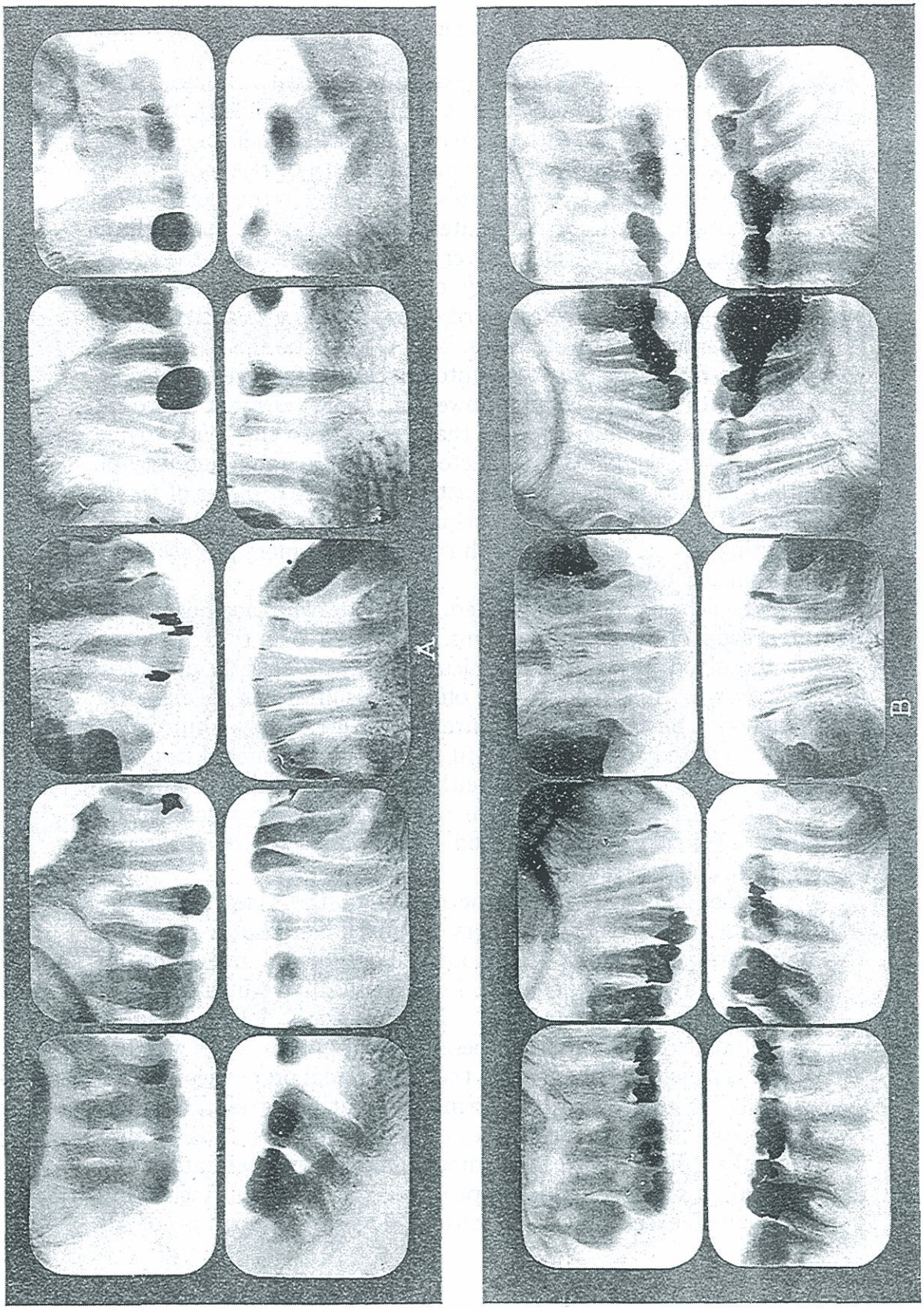


FIGURE 246. BACTERICIDAL PROPERTIES OF BLOODS: A, NORMAL HUMAN; B, BROKEN DEFENSE; C, BROKEN DEFENSE PLUS TOOTH TOXIN.

ten to thirty minutes, the living organisms were then placed in it for given periods of time; and it is quite remarkable that many individuals show a greatly increased activity of their blood from the presence in the blood of a small quantity of the tooth toxin prior to, if only for a few minutes, the placing in the blood of the living organisms for ten minutes. The bloods of some other individuals, however, make a very little response from the tooth toxin as an increased activity or efficiency. There is also a quantity factor. If the blood receives so small a quantity of the toxin as would be transferred to it by placing the tips of the roots of a freshly extracted tooth into the blood for ten minutes, a blood with a good reacting power will show a distinct improvement over the blood without that exposure to the tooth toxin. If, however, the blood is subjected to a considerable quantity of this toxic substance, such as putting the crushed pieces of tooth into the blood for an hour, it frequently practically paralyzes this reacting power, and the growth is many times more profuse than if a smaller quantity is used.

When the sterile, defibrinated, freshly drawn blood has placed in it some of the dead organisms, as stated above, their presence in the blood furnishes a chemical which acts directly upon the leucocytes, which quickly give off, as a result of this chemotactic reaction a bactericidal substance of very great power but which is not yielded to the blood until the stimulus is offered from the living or dead organisms, and either will accomplish the purpose. There is, therefore, an amount of dead organisms which will be most efficient for a given blood to induce it to its maximum bactericidal reaction.

In Chapters 3, 4, and 5, the results of the researches have indicated that there is a very distinct difference in the local structural changes in the mouth about dental infections, in patients having a low defense, from the reaction which occurs in the mouths of patients with a high defense. I have desired, therefore, to check carefully these different groups to see whether there is a distinct difference in the bactericidal properties of their bloods. It is necessary to keep in mind that, while all individuals may tend to have a mien, they may depart quite considerably from that mien. I have, accordingly, selected two patients on the same day, one presenting for prophylactic care. During his life he has had exceedingly little caries. The roentgenograms of his


A
B

case are shown in A, Figure 247; and it will be noted that he has very extensive pericdontoclasia. His age is about forty-five. He has never had any of the rheumatic group disturbances, nor have the members of his family. He is, accordingly, a typical illustration from the family history, his own history, and the local dental pathology, of the group with a high defense or absent susceptibility. His case number is entered as 1415.

The other patient (No. 1414) presents with symptoms of mild heart involvement, nervous exhaustion, and some neuritis. The roentgenograms of her teeth are shown in B of Figure 247. It will be noted that she has little tendency to gingival recession. However, she is young, her age being seventeen. She has several pulpless teeth, and notwithstanding a considerable quantity of pulp chamber unfilled, there is not extensive absorption of alveolar bone. In Chapter 43 I have shown the picture of the heart of a rabbit, inoculated with a culture from one of her teeth, having both endocarditis and myocarditis. This patient's father has had serious similar involvements, and his case is reported in Chapter 22.

I have, accordingly, undertaken to compare the defensive efficiencies of both of these bloods for combating streptococcal infection taken from dental source. The result is most striking and really remarkable, as shown in Figure 248, which shows two rows of Petri dishes, four for each of these two patients. The top two, marked A, are Petri dishes containing an agar culture medium suitable for growing streptococcus, planted with approximately one thousand streptococci. These are the controls. The other Petri dishes had the same quantity of the same kind of culture medium—namely, 15 cc.— and the same quantity of live organisms in each case except as follows: In B, before placing the thousand organisms in the Petri dishes they were subjected for ten minutes to contact with one-fourth of a cubic centimeter of the blood of one of each of these two patients. The germs and blood were then put into the Petri dishes which contained fifteen cubic centimeters, and as the germs were carried in approximately one-thousandth of a cubic centimeter of fluid, the additional fluid added to the Petri dishes in B was insignificantly more than in A, and the additional nutrient material only that quantity in a quarter of a cubic centimeter of blood.

It will readily be seen that Patient 1414, classified as an inherited susceptibility, did not furnish a blood capable of destroy-

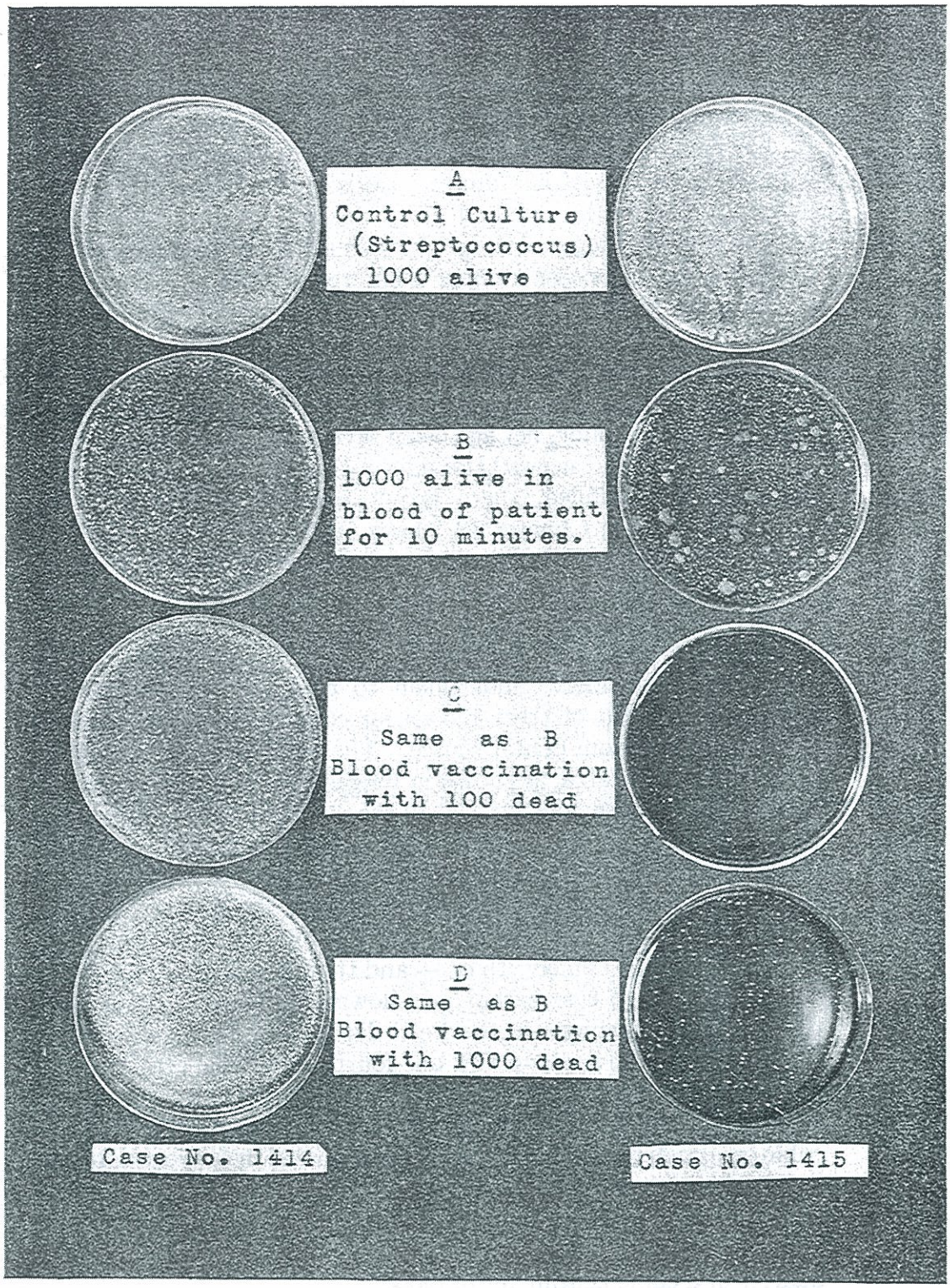


FIGURE 248. COMPARISON OF BACTERICIDAL CAPACITY OF BLOODS OF TWO PATIENTS PRESENTING SAME HOUR. CASE NO. 1414 HAS LOW DEFENSE WITH HEART INVOLVEMENT; CASE NO. 1415, WITH HIGH DEFENSE AND NORMAL. (SEE DENTAL CONDITIONS IN FIGURE 247.)

ing a very large number or proportion of the approximately one thousand organisms; but in strong contrast with this, the patient with the absent susceptibility, Case No. 1415, was able to destroy a large portion of the one thousand organisms with even that small quantity of blood in the remarkably short time of ten minutes. This we might take to represent the readily available resources of the blood for meeting an invading infection. But, as has been shown, the blood has normally a very high reserve defensive mechanism stored up in the leucocytes, which is capable, when called forth, to take care of very much larger numbers of organisms. I have, accordingly, then, endeavored to determine the relative capacity of these two individuals as representatives of their groups, for meeting an overwhelming or large infection, by placing in the same quantity of their bloods *in vitro* a given number of dead specimens of the same organism which we are using for testing. In C we have the effect on this quantity of organisms—namely, one thousand alive—by being placed in the blood of one of these two individuals for ten minutes as before, where the blood had been vaccinated for twenty minutes preceding with one hundred dead streptococci of that strain. It will be noted that the blood of Patient 1414 did not have the capacity for any greater response since more of the organisms of a thousand grew out than when the blood was not vaccinated, whereas the patient with the high defense, according to our classification by other means and by clinical histories, is shown to be correctly named, for the addition of these few dead organisms has called forth from his blood a chemical reaction which has devitalized practically every one of the thousand organisms in the small space of time of ten minutes.

We might assume, then, that Patient 1414, with low defense, did not respond because the vaccinating dose was not large enough. We, accordingly, made simultaneously with the preceding test, a determination of the effect of vaccinating for the same period—namely, twenty minutes—with one thousand dead organisms per one-fourth cc. of blood, in order that for every organism that was to be devitalized, one dead organism would be placed in the blood as an antigen to call forth that quantity of antibody. The blood of the patient with a low defense was not capable of responding to a greater degree with this relatively large vaccination, for, in fact, her blood destroyed many fewer organisms than without the vaccination, and there seemed distinct evidence

that the additional toxic effect of the thousand dead organisms embarrassed her blood to a marked degree, for when we compare the growth in D with that in A, we find her blood had almost lost its capacity for destroying bacteria, at least in that unit period of time. The patient presented in the other column, No. 1415, has been able to destroy almost all of the thousand organisms, but a few are growing, indicating that the toxic additive quality was sufficiently great to reduce the efficiency appreciably, since there was not approximately 100 per cent devitalization of the bacteria, as shown in C. We have, therefore, a type of evidence which substantiates the deductions in the preceding chapters, and I see no other explanation for the conclusion that the group of individuals represented as having the capacity for doing what Patient 1415 has done as compared with what 1414 has done, than that we are dealing with potentially two entirely different capacities for defensive reaction.

This illustrates too why the indiscriminate use of vaccines may have a very harmful effect in some instances while being distinctly helpful in others. Let us suppose that Patient 1414 had had a vaccine used in which the dilution and dosage was either of those represented, and probably any dilution between them. It would be almost certain that the vaccine would do more harm than good and that the patient would be made distinctly more ill. On the other hand, we readily see that if the patient in the second group received a vaccinating dose of either of these quantities, or probably any quantity between, his defensive mechanisms would be distinctly sharpened. As suggested, therefore, this becomes a means for determining *in vitro* those individuals for whom a vaccine may be expected to be beneficial and those for whom it will be injurious; and still more, by an extended series of these determinations, the particular dosage that will be most efficient for that individual can readily be estimated. This, therefore, should remove in the future much of the indifferent and negative result from vaccine therapy, and, as previously stated, we are indebted to Sir Almroth Wright for the development of this and much of the bacteriological and serological knowledge regarding the blood and its defensive mechanisms. The references to his work are very many and I have given the principal ones in the bibliography.

SEROPHYTIC MICROÖRGANISMS.

PROBLEM: What are the growth factors of microörganisms of the mouth in juices of living tissues?

EXPERIMENTAL AND DISCUSSION.

We naturally think of all of the forms of microörganic life as possible invading factors. It seemed wise to determine, if possible, to what extent the natural limitations of the various types of organisms would prevent their growth in normal tissue juices, assuming that dental infections are continually in contact with abraded tissue and that various forms of organisms have an opportunity to invade the vital structure. Since one of the first mechanisms of Nature's defense, when tissue is abraded, is to throw out the lymph, it is suggested as important to determine, if possible, which of the mouth organisms will grow in that fluid. I have, accordingly, placed sterile absorbent cotton beneath the skins of normal animals in order to collect a sufficient quantity of this material for experimental purposes. I have also obtained the same material by slow suction from the human. This material has been infected with mixed organisms of the mouth, including spirochetes, fusiform, long and short rod forms, micrococci, subtilis, diplococci, streptococci, and staphylococci. It is of great importance to note that almost invariably, so nearly so that it may be considered a constant rule, when animals are inoculated with mixed cultures, in many of the above varieties the only organism that is recovered from the lesions will be of the coccal group, and in more than 99 per cent of cases in our studies of the diplostreptococcal groups, there being less than 1 per cent staphylococcal infection also. It is not surprising, therefore, that when the human or animal lymph is inoculated with the mixed infection of the mouth, the streptococci and staphylococci grow out in the lymph of susceptible species or individuals, particularly the former, while the bacillary forms and spirochetes do not multiply, or at least do not in sufficient quantities to be found in the smears or tissue sections.

This research has been undertaken for two purposes: First, to determine what organisms tend to grow most readily in freshly extracted lymph and, second, as a means of comparing the lymphs of different animals. The table shown in Figure 249 shows a series of rabbits and rats in different conditions. Rabbit 1202 had sterile absorbent cotton placed beneath the skin for two hours, when it was removed and a couple of cubic centimeters of

LYMPH EXPERIMENT

	Lymph Dilution	Days Growth 1st Smear	Strepto-cocci		Bacilli		Days Growth 2nd Smear	Strepto-cocci		Bacilli		Days Growth 3rd Smear	Strepto-cocci		Bacilli	
			Gram-Positive	Gram-Negative	Gram-Positive	Gram-Negative		Gram-Positive	Gram-Negative	Gram-Positive	Gram-Negative		Gram-Positive	Gram-Negative	Gram-Positive	Gram-Negative
Rabbit No. 1202	Undiluted	1	—	—	—	—	2	+	—	—	++	10	++	—	—	+
	Dilution 1:5	1	+	—	+	—	2	—	+	—	—	10	++	—	—	+
	Dilution 1:1	1	++	—	—	+	2	++	—	—	—	10	+++	—	—	+
Rabbit No. 1222	Undiluted	1	—	—	—	—	2	++	—	—	—	10	+++	—	—	+
Rat-Normal Diet	Undiluted	1	—	—	—	+	4	+	—	—	+	6	+++	—	—	+
Rat-Deficiency Diet	Undiluted	1	+	—	—	++	4	+	—	—	++	6	+++	—	—	+
Rat-Deficiency Diet	Undiluted	2	—	—	—	++	3	±	—	—	++	4	+	—	—	+
Human Serum Case No. 335		2	++				10	++++								
Case No. 1421		2	++				10	++++								

FIGURE 249.

lymph expressed into sterile tubes. Dilutions of one to five, one to one, and full strength, were tested, as was lymph similarly drawn from Rabbit 1222, by inoculation with the mixed flora from highly infected gingival pockets. The chart shows three different succeeding dates and the type of streptococcus, whether positive or negative, and the type of bacillary form, whether Gram-positive or negative, which grew out. It will be noted that the undiluted lymph from the two rabbits gave no growth in twenty-four hours, whereas the dilution of one to five gave a slight growth of Gram-positive streptococci and of Gram-positive bacilli. The forty-eight hour culture, however, showed Gram-positive streptococci in both the undiluted and a Gram-negative bacillus in the other. The ten day growth showed a more abundant Gram-positive streptococcus and diplococcus, and Gram-negative bacilli. The organism, however, which grew out in the majority of instances and most profusely, was the Gram-positive streptoccccus. The three rats—shown in the same chart,

CHANGES IN RATS WITH PLANTED TEETH—NORMAL AND DEFICIENCY TEST

	Diet		Original Weight at Inoculated Date	Weight Changes						Days Tooth Retained		
	Normal	Deficiency		3 to 4 Days	6 to 7 Days	8 to 9 Days	10 to 11 Days	15 to 16 Days	20 to 25 Days	Normal	Deficiency	
Group I Normal Diet	+		122	120	110	119	122	139	173	**6**		
	++		192	179	185	187	186	194		**9**		
	+		124	126	127	129		133		**13**		
								Average		**9**		
Group II Deficiency		+	79	86	90	91	95	93	106		**40+**	
		+	84	87	91	92	88	96	101		**40+**	
								Average			**40+**	
Group III Pregnancy			139	136	135	140	134	142	134		**6**	
			184	186	123	122	125	129	149	**9**		
			285	291	239	244	222	230		**14**		
								Average			**9**	

FIGURE 250.

had lymph removed in the same manner, and it will be noted that in general the same condition obtained though the growth was exceedingly weak at first. We find ourselves unable to determine when an infected lymph has degenerated to a point where it ceases to be comparable to normal circulating lymph, and it is probable that after twenty-four hours it should be considered that its bactericidal properties would be greatly reduced. In the study of the rats, however, it will be noted that the second rat serum showed a Gram-positive streptococcus in twenty-four hours, but it may be significant that this rat was on a deficiency diet, as compared with the one preceding which was on normal diet. There is also a greater growth at the end of twenty-four hours in the Gram-negative bacillary forms in both the rats on deficiency diet.

These and other results suggested the desirability of repeating on the rats some of the experiments that had been made on rabbits by the implantation method. The table in Figure 250 shows a series of these results. Teeth were implanted beneath the skins of rats, and their weights were taken on succeeding days. The results are strikingly different from those which were obtained by placing similar infected teeth beneath the skins of rabbits. It may be argued that a human tooth is a relatively

large quantity of infection to place beneath the skin of a rabbit, the quantity effect, therefore, accounting for the high mortality from that operation. If this quantity factor be true of the rabbits, it must of necessity be infinitely more true of the rat, which is approximately one-tenth the weight of a rabbit. It is most interesting to see, however, that in practically every instance these infected teeth have produced practically no serious effects on the rats when they were on normal diets, as estimated by their change in weight, for they have gone on gaining quite like the controls. The only difference discernible has been that they are not so active in their cages, tending to sit quietly in a corner, and this is particularly true of those on deficiency diets. When we compare, however, those rats that were on a deficiency diet, with those on a normal diet, there is a marked difference.

When an infected tooth is placed beneath the skin of a rabbit, the reaction almost immediately resolves itself into one of two processes: either there is formed a capsule, highly vascularized and which apparently acts as the defensive mechanism built about the structure, in which case the rabbit lives, or there is a more or less active local degeneration accompanied by very definite changes in the ionic calcium of the blood, the alkali reserve of the blood, the ratio of polymorphonuclears to lymphocytes, etc. In exceedingly few cases, however, does a rabbit ever expel by a local suppurative process the infected tooth so planted. On the contrary, however, rats with their higher defenses will build an encapsulation about the tooth, break down a gateway to the surface in an astonishingly short period, as shown in the chart in Figure 250, in which it will be seen those rats on a normal diet shown in Group 1, have expelled the tooth in from six to thirteen days, with an average of about nine days. The rats on a deficiency diet, however, (see Group II) required over forty days on an average to expel an infected tooth. In Group III, we have undertaken to get data that would enable us to make comparisons between rabbits and rats with regard to their defense at the time of pregnancy and the effect of such a foreign implantation in that condition. The data available are not sufficient for extended conclusions. In general, however, pregnant rats did expel infected teeth about as rapidly as did the rats that were not pregnant. In the chapter on overloads I have shown that when rabbits are injected with dental cultures during pregnancy, there is a tendency to abortion or to the death of the fetal forms, with or with-

out the expulsion, and with great danger to the life of the mother rabbit. Since the period of gestation with rats is so short—namely, three weeks—it is exceedingly difficult to determine whether the effect of tooth implantations tended to hasten confinement. The effects are distinctly different, however, on rats than on rabbits, since the offspring of pregnant females carrying implanted teeth seem to be normal and develop as though no such overload had been placed upon them, whereas with rabbits, results were nearly always fatal to the offspring. They were either stillborn or lived but a few hours. A typical illustration of this effect is shown in Figure 251, in which will be seen two rats in the backs of which infected teeth were planted. One has completely expelled the tooth in nine days, and the other in thirteen. In the latter, however, the tooth is just in the process of exfoliation.

SUMMARY AND CONCLUSIONS.

1. While this study is, as yet, very incomplete, sufficient progress has been made to indicate that there is a very great difference in the defensive mechanisms of different species of animals. From these studies and from determinations made by the method presented, it is apparent that the rabbit and rat have distinctly different capacities for defensive reactions to dental infections.

2. The bactericidal property of the blood and lymph of rabbits was very similar to that of the human, though under normal conditions apparently not subject to so great variations.

3. The organism which tends most readily to grow out in the lymph and blood serum of humans and of animals, is a Gram-positive streptococcus, which corresponds to our studies reported in other chapters regarding the organism isolated from involved tissues of animals which have been inoculated with mixed cultures from human dental sources.

We see from the above that there is a great variation in the bactericidal properties of different bloods, whether of animals or humans, and that this quality of high or low defense relates directly to our groupings of individuals with or without systemic involvements from dental and other focal infections, and that the bactericidal quality can express itself in even one minute's time to such a marked extent as to destroy a large proportion of the organisms exposed to the blood. We would, therefore, briefly express this quality in the following conclusion:

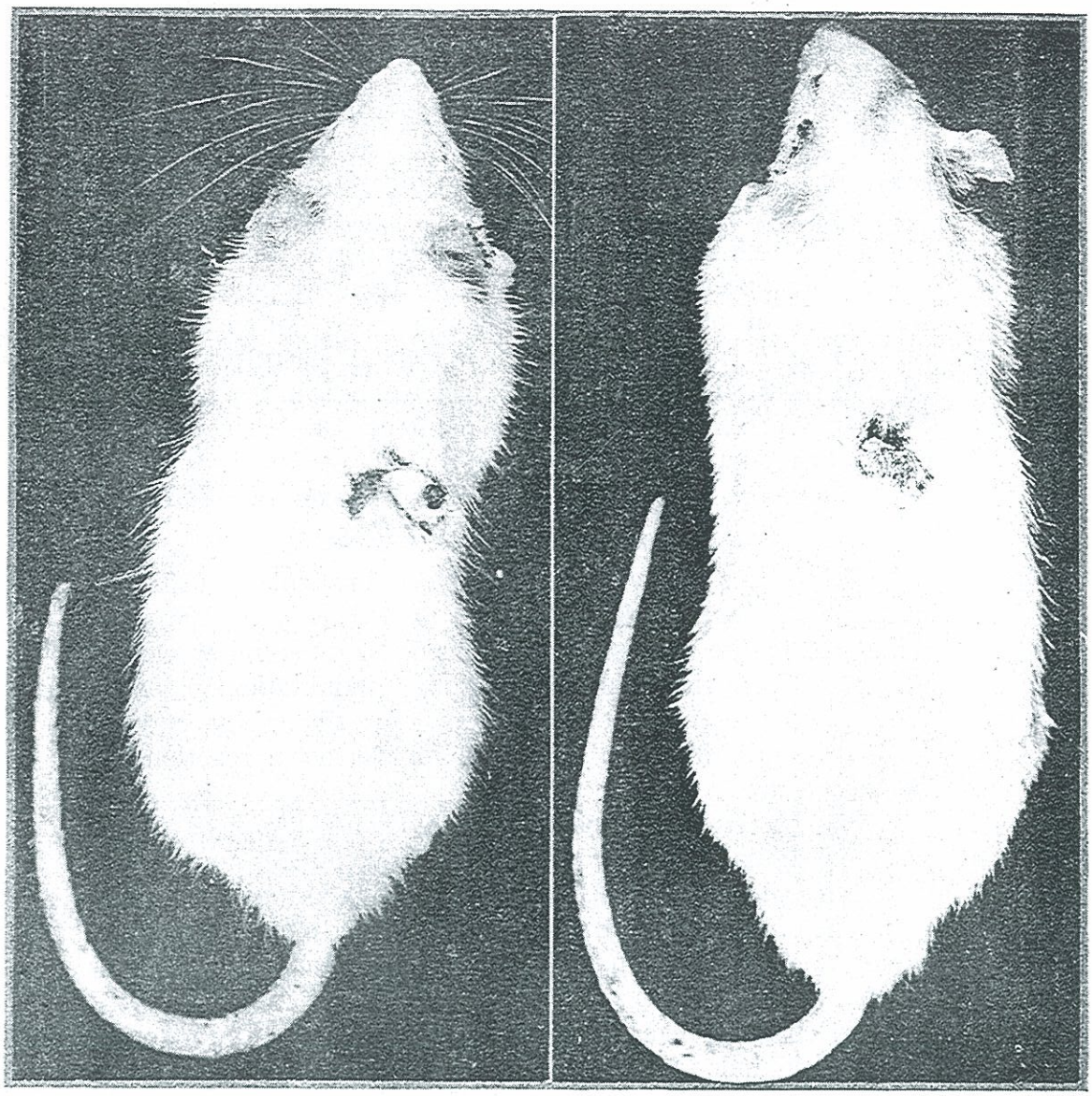


FIGURE 251. TWO RATS WITH TEETH PLANTED BENEATH THE SKIN, ONE COMPLETELY EXTRUDED AND THE OTHER NEARLY SO. THEIR HIGH DEFENSE MAKES THIS POSSIBLE.

There is a marked difference, which is very readily measurable in the bactericidal properties of the bloods of individuals of high defense, as compared with those of low defense to systemic involvements from dental infections.

When the mixed flora of the oral cavity is planted in the normal blood serum or lymph, the varieties that grow are almost entirely limited to the strains of diplo- and strepto-cocci, with occasional staphylococci, with the diplo- and strepto-cocci largely predominating.

CHAPTER XLII.

METHODS FOR REINFORCING A DEFICIENT DEFENSE.

PROBLEM: Can a temporarily or permanently low defense against the streptococci of dental infections be increased or enhanced either temporarily or permanently?

EXPERIMENTAL AND DISCUSSION.

In the preceding chapter we have seen first that there is a great variation in the defensive factor of different individuals as expressed in the bactericidal property for streptococci of dental origin, and also that this quality regularly diminishes in rabbits when they have been subjected to implantation of infected teeth. The researches there reported also indicate that the defense of an individual tends to go up with the removal of chronic dental infections. But many of our patients do not come back readily to normal. If a sapling be broken over, it may straighten nearly to its original position. If, however, it can be supported, as being tied to a stake, it much more rapidly will repair the injured timber and probably recover its original strength. Just in proportion, however, as that sapling may have been held crushed over to the ground for a long period of time, or its defensive factors injured by any other means, the prospects for a complete recovery are rapidly diminished; and if it should be that the timber in question is that of an old tree, the repair may be much less vigorous, and the obstacles that will be safely overcome much less, than with the young tissue.

Similarly, many of our patients come to us with overloads that have been present for so long a time that, even though they are removed, the defense is very greatly lowered. In many instances the overload is one that cannot be reached or removed, and it therefore cannot be subtracted. In still others the overload consists of an inherited deficiency in the mechanisms of defense, for we have seen in the preceding chapter that the individuals constituting our first group in susceptibility—namely, those with absent susceptibility—have by inheritance a high defense, and they show an unusually high bactericidal property of the blood.

In the second group—those with an acquired susceptibility—while in that state we find that they have a lowered defense below their normal at other times, but that they tend to come back to their normal with removal of overloads. In other words, the bactericidal property of their blood is temporarily depressed by their overloads, one of which overloads is very often a dental infection. The third group—those with an inherited susceptibility—always have an abnormally low defense against streptococcal infections; and their normal, which is poor at best, tends readily to be still more depressed with overloads. They are in a state in which the normal unstimulated defense of the blood is not adequate to protect them against streptococcal and staphylococcal invasions. In the recurring active combats with this type of infection, as any of the rheumatic group lesions, they whip themselves up to a defensive reaction adequate to make them temporarily relieved. They are, however, dependent upon this secondary defensive mechanism which must be called into play frequently and vigorously, and, accordingly, they have what they call attacks of their disturbance which are largely records of remissions and exacerbations.

When, in any individual the normal defensive mechanism is not adequate and the infection continues to develop and increase in quantity, the very increase, which endangers the host, is the mechanism which sets in motion the defensive machinery constituting the secondary defensive systems of the patients. These secondary defenses are largely in the blood and tissue cells of the body, probably mostly in the leucocytes of the blood. For years as we have studied these patients with their chronically low defenses, we have realized that the desideratum in their behalf was to find some reinforcement which could be brought to their aid to supplement their defensive systems. We readily visualize how the antitoxin for the diphtheria toxin is developed by the horse and can be readily transferred from the horse's blood serum to that of the patient, with the result that a sufficient reinforcement is added to turn completely the tide of the events; and the individual whose death was certain or life despaired of, because of his losing the fight with that organism, finds the table turned, and thanks to the defensive substances contributed by the horse, the patient is now able to make a winning fight and the organisms are annihilated from his system or rendered so innoxious to him that the body ignores them, in which case he may become a carrier.

But the toxin developed by the diphtheria bacillus is an exotoxin, and the streptococci and diplococci with which we are concerned develop largely endotoxins, and it is a very different matter to produce outside the body of the host a substance which will be bactericidal or antitoxic of such a degree as to make a comparable reinforcement to that made by the diphtheria antitoxin. Indeed, we seem to be dependent upon bactericidal substances that are generated within the blood and tissues of the host for defense against this organism. We, therefore, come back continually to the program of using vaccines, preferably made from the particular strain of organism that is producing the disturbance. I have been using these autogenous vaccines for over ten years with very variable results. In many instances the vaccines seem to have little, if any, beneficial effect; and, indeed, in a few cases they seem to be positively to the patient's disadvantage, while in other cases they seem to work like magic. With their use many patients have been seen to make a most definite increase in the rapidity of their mastery over the invading infection. Several of these are discussed in the chapters on systemic involvements; and in several instances where patients had been either completely or nearly bedridden for years, they have been put back on their feet by changes that have been produced, apparently, by the removal of dental focal infections and the stimulating of their lowered defenses by use of a vaccine.

To be more specific, the patient shown in Chapter 64 had been bedridden for five years with deforming arthritis. The removal of her dental infections produced but little change. The use of the vaccine made from those dental infections made so great improvement that she was on her feet in five months' time, and for two and one-half years she has had no recurrence sufficient to put her back in bed. She now does all her housework except the laundry. This result was produced with an autogenous vaccine.

Similarly, the case shown in Chapter 64, who had been bedridden for four years, completely helpless, has now for several years been doing her housework, and continues practically free from rheumatic disturbance and progressively improved, apparently largely the result of the vaccine together with the removal of the dental infections.

Similarly, we might review many cases. Note that while many cases have responded beneficially to the use of a vaccine, many others have shown no improvement, and this we were able

to determine only after trying and failing. All of this has suggested that ultimately we must find some substance which may be added to the patient's defensive mechanism and thereby help him or her directly to combat the infection. Again we are greatly indebted to Sir Almroth Wright for splendid suggestions, for he has shown that this process of vaccination of the blood is quite as effective *in vitro* as *in vivo*; and we have, accordingly, taken that suggestion and tested the bloods of the patients presenting for diagnosis and means of assistance in the defense against their infections.

In general, we find that while there is a great difference in the response of the blood of different individuals, they tend, in general, to show a capacity for a greatly enhanced bactericidal efficiency of their blood by the introduction first into their blood of dead organisms, we now think preferably of the strain for which the bactericidal quality is being determined. The difference in different patients is so great, that whereas a very few dead organisms will suffice to call forth from the blood this secondary defensive factor in some cases, in other cases a larger quantity of dead organisms are required to do so. There is also a very great difference in the extent of this reinforcement for secondary defense, as determined by the number of organisms that will be killed by a given blood after being vaccinated *in vitro* with varying amounts of dead organisms of the same strain. The blood of some patients reaches its maximum efficiency with the addition of a very few dead organisms per unit volume, where others do not have the maximum efficiency called forth until a large number of dead organisms are added; and, similarly, whereas some bloods will kill off a large per cent, or nearly all of the living organisms, they are aided after being vaccinated, whether that quantity of live organisms be five per cubic centimeter or five thousand, or even fifty thousand, some other bloods will reach their maximum capacity with a few hundred bacteria. In other words, there is a very great difference in the capacity of different bloods for reaction, as well as a very great difference in the quantity of dead organisms that are required to produce the most efficient reaction.

MEANS FOR COMPARING AND CLASSIFYING THE DEFENSIVE FACTORS OF PATIENT'S BLOOD.

Since, as we have shown, there is a very great variation in the bactericidal property of these various patients, when considered

individually, and in the groups when considered as such, it becomes very desirable to evaluate this defense in comparative terms. This has suggested the development of the system of uniform observations and determinations to be made on various individuals being studied, in order that we may establish, ultimately, a group of standards which will express the limits that may be placed on both an adequate and inadequate defensive mechanism. After working out several combinations of tests and controls, the one that we are using at the time of this writing as being the most simplified to date, is shown in Figure 252. These forms are used as the outline for the different determinations and the results are checked directly into them, and they lend themselves to modifications when such are desired. The Petri dishes are numbered in accordance with the numbers in the column to the left, and we soon come to know what tests any given number represents.

All of the study of this phase of our problem—namely, the mechanisms of defense of the blood and the means for their strengthening—have suggested the necessity for the development of other means than the use of vaccines for the strengthening of the defense. To do so has required further knowledge of the nature and structure of the substances chiefly instrumental in elaborating or generating these defensive factors. Wright has shown, as we have repeatedly verified, that the simple process of heating the vaccinated blood before its vaccination with the dead organisms entirely inhibits the enhancement of the bactericidal property, and this because the leucocytes are devitalized at 48° C. It is therefore possible to determine very exactly and directly the amount of the defensive substances already in the blood before a reinforcement is drawn from the leucocytes. We have, accordingly, demonstrated that in some individuals with a chronically low defense the amount of defensive element present in the blood, without calling forth any material from the leucocytes, is exceedingly low, and in some others we find that the leucocytes tend to contribute this reinforcing immunity with a small amount of stimulation from the presence of dead organisms or from toxin, while others require a much larger quantity of stimulation. Another and most striking feature which we referred to in the preceding chapter is the fact, that most bloods of a high defense will develop this secondary defense within one minute after the placing of the tooth toxin or

BACTERICIDAL POWER OF BLOOD

Patient Case No. Date

Serial No. of Plate	Patient	Blood			Media		Vaccinated Dead Organisms and Time Exposed			Live Organisms and Time Exposed			Tooth Toxin			Results
		Normal Control	Quan Used drops	Quan Used cc.	agar	other	100 50	1,000 500	10,000 5,000	100 50	1,000 500	10,000 5,000	Patients	Misc.		
1	√		2		√											
2		√	2		√											
3					√					Ctl						
4					√						Ctl					
5					√							Ctl				
6					√		Ctl									
7					√			Ctl								
8					√				Ctl							
9	√			1	√					10						
10	√			1	√						10					
11	√			1	√							10				
12		√		1	√					10						
13		√		1	√						10					
14		√		1	√							10				
15	√			1	√		20			10						
16	√			1	√			20		10						
17	√			1	√				20	10						
18	√			1	√		20				10					
19	√			1	√			20			10					
20	√			1	√				20		10					
21	√			1	√		20					10				
22	√			1	√			20				10				
23	√			1	√				20			10				
24		√		1	√		20			10						
25		√		1	√			20		10						
26		√		1	√				20	10						
27		√		1	√		20				10					
28		√		1	√			20			10					
29		√		1	√				20		10					
30		√		1	√		20					10				
31		√		1	√			20				10				
32		√		1	√				20			10				
33	√		2		√								30			
34	√			1	√					10			30			
35	√			1	√						10		30			
36	√			1	√							10	30			
37		√		1	√					10			30			
38		√		1	√						10		30			
39		√		1	√							10	30			
40																

FIGURE 252.

dead bacteria from same, whereas the blood of other individuals will require several minutes (ten to fifteen) to develop the defensive factors. We have also found that this quality varies through considerable range whether a rabbit is normal or has been under the strain of a dental infection such as the planting of an infected tooth for some days. This latter indicates to us that the presence of the dental infection has decreased the capacity of the leucocytes for reaction, as well as the important data brought out in Chapters 19 and 20 showing that the presence of the infection reduces the number of leucocytes or produces a leucopenia, chiefly a depression of the polymorphonuclears, and also depresses the ionic calcium of the blood. All of this has suggested that the whole problem resolves itself very largely, if not quite entirely, to one of chemotaxis.

In this connection we think immediately of the capacity of certain drugs to act specifically on certain infections. This is quite strikingly illustrated in the effect of quinine on the malaria plasmodium, and of the arsenic compounds, such as salvarsan, on the Treponema pallidum. We also think of the action of the salicylates which have been used so extensively in the treatment of rheumatic affections. I will, accordingly, report here under the studies of the mechanisms for the increase of defensive mechanisms of blood, some studies we have made with the salicylates.

Some years ago I inoculated two groups of rabbits with proportional amounts of a culture producing acute rheumatism, and treated the one group with the sodium salicylates and the other without. I was never sufficiently satisfied with the results to publish them, since I could not interpret them. The evidence indicated that the rabbits receiving the sodium salicylate of the doses I was using lived longer, but with reinoculations with the same strain, the evidence suggested that a larger percentage of the rabbits developed heart lesions. I was never able to determine whether the test had important significance since there were no data on what should constitute a proper and what an overdose of that drug for rabbits, and it would be very clear that any overload, such as an overdose, might be distinctly harmful.

More recently I have had an opportunity to make a different type of study directly on the human. A patient with acute deforming arthritis presented for our study, reporting that he had been getting progressively worse, that the only drug that seemed

to give him any relief was some form of salicylate, and that he had come to the point that even this had to be taken in such large doses that its continuance seriously disturbed his digestion, and that his physician was now administering it intravenously three times a week. I suggested to him that before anything was done to disturb dental infections or any other of the factors involved, we make studies of the changes in the ionic calcium of the blood, if any, accompanying and following the intravenous injection of the sodium salicylate. Results were most striking. The ionic calcium of his blood at the time was running at approximately 7. With each intravenous injection the ionic calcium of his blood would drop to the neighborhood of 6, and in about twenty-four hours it would ascend to 9 or above, and in another twenty-four hours would return to about its original level.

Coincidentally, there was a parallel change in his symptoms. Within an hour after the intravenous injection of the sodium salicylate by his physician, sometimes within thirty minutes, (for he came directly, according to our mutual arrangement, from one office to the other, a distance of a few blocks,) he developed a profound depression amounting to a rather extreme negative phase. This usually lasted for about five hours, when it gradually disappeared and in its place came a sense of well being, great relief from his rheumatic symptoms, and with it a displacement of the mental cloud with one of hope and confidence and general well being. This latter usually lasted about twelve hours, after which he gradually subsided to his old level. The history of his case was very similar to that of general clinical practice: namely, that the symptoms as pain were greatly relieved by the use of the salicylates; that the system needed to be pretty well saturated to develop this reaction; that the results were relatively transient, requiring quite frequent and continuous repetition. We have, therefore, in this case an illustration of the direct effect of chemotaxis in influencing the defense and also indicate one, at least, of the changes occurring in this patient's blood. We were not at the time of this series of determinations making bactericidal determinations of the blood. This has since been done, for he is still suffering and almost an invalid with his deforming arthritis. The changes in the ionic calcium of this patient's blood, as shown by the various determinations

IONIC CALCIUM, SODIUM SALICYLATE, AND DIET FACTORS

Date	Sugar	Non protein Nitrogen	Uric Acid	Biological Determination				Chemical Determination	
				Calcium Ionic	Calcium Ionic and Combined	Calcium in Combination	Thrombin	Calcium	Alkalinity Index
8–17–22					10.625				
8–24–22				6.67	9.81	2.14			
8–24–22				7.85	8.34	0.49			
8–24–22				**10.00**	**11.11**	**1.11**			
8–26–22				**5.51**					
8–28–22				7.49					
8–28–22				6.67					
8–28–22				6.34	8.76	2.42			
9– 2–22				6.67	9.02	3.55			
9– 5–22	105	47.5		6.67	9.33	2.66		10.87	
9– 8–22				6.68	9.72	3.04			
9–11–22				7.27	8.73	1.46			
9–13–22				7.52	9.52	2.00			
9–19–22				7.00	9.23	2.23			
9–21–22				8.10	9.87	1.77			
10–18–22				7.54	12.08	4.54			23.3
11–23–22					12.82		12.68		
12– 8–22	103		3.25		12.10		13.46		
3– 7–23	93	26.5	2.85	12.206	14.34	2.85	6.79		
4–19–23	95			12.061	13.34	1.279	6.539		

FIGURE 253.

are presented in Figure 253. It is important to note that after this patient went on a forced milk diet, taking large quantities, his ionic calcium has increased from a level at about 8, frequently being as low as 6 and a fraction, to 12; and while, when last seen, he thought his general condition was somewhat improved, his actual improvement has been slight; and it is apparent that the depressed ionic calcium of his blood is not the principal factor in his lesion. The bactericidal property of his blood is exceedingly low, and the condition strongly suggests that if some bactericidal element could be used to reinforce his own normal defense, he would make much more rapid progress. He has had dental focal infections removed with but little improvement in his general condition. He has had vaccines used and these do not call forth the needed defensive response from his blood. He seems quite unable to manufacture the bactericidins required for defense against this infection. Since the removal of his dental infections, he has been under treatment for chronic colitis, which has existed for years and which is undoubtedly contributing to his general condition, and, indeed, it is not improbable that the infection there is furnishing a toxin which is destroying his defensive mechanism or neutralizing its efforts. I have

reviewed this case in this detail to illustrate a condition which exists in a very large number of the patients with marked rheumatic susceptibility, and thus emphasize our limitations and thereby stress the need for more intensive effort.

Another means of approach to this problem has already been discussed in the chapter on the Glands of Internal Secretion, and it has been instructive to find that whereas a given tooth from one of our patients, at the time of this writing has killed thirty-three rabbits in an average of four days, the use of injections of extract of parathyroid not only seemed to increase the resistance of the rabbit, as judged by the length of its life which was ten days (only one other rabbit in the series having lived to that length and it an unusually large one) but perhaps more important, following the injections of the parathyroid, this rabbit's ionic calcium was increased, for, whereas in other rabbits the ionic calcium progressively decreased quite continuously and regularly, this rabbit's calcium, which was 7.2 before the injection, increased to 10 the following day, which change occurred on two different occasions. This has suggested quite strongly, since this parathyroid was injected subcutaneously around the implanted tooth, that there may have been a local reaction between the parathyroid substance and the toxic material of the tooth. Studies are now in progress to throw further light on this phase of the question.

It is of particular interest to note that we have frequently seen in individuals a very prompt increase in the ionic calcium of the blood from the administration of parathyroid and calcium lactate, one or both. Such cases are cited in the chapter on the Glands of Internal Secretions. In one case, for example, in two weeks' time the ionic calcium of a woman suffering from rheumatism increased from 8 to 10, and in the two weeks' time her depression and discouragement had completely given way to one of cheerful confidence and joy of living, together with relief of the rheumatic symptoms. It must be stressed that this work is still in the experimental stage and the members of the profession must not rush headlong into the administration of this and other drugs until further experimentation under controlled conditions shall have been made.

For considerable time I have been making studies with other drugs to ascertain, if possible, whether or not beneficial results might justify their use for reinforcing an abnormally low human

defense. I have found two drugs in particular to be apparently helpful in increasing the defense of rabbits. One of these, ethylhydrocupreinhydrochlorate, enabled the rabbits that had been prepared by its use to withstand approximately eight times the lethal dose of infection when inoculated intravenously. Some of these rabbits, however, developed untoward symptoms, particularly in the rabbits' eyes. I have since learned of work that has been done with this drug by different observers in the treatment of pneumonia, some of which patients developed eye complications, and there has been a difference of opinion as to the extent to which this drug was involved in the secondary involvement. Another drug which has been studied is the active principle of chaulmugra and its compounds. These have been reported in Chapter 26 on Chemotaxis. It is sufficient to state at this point that these drugs, while showing promise and encouragement for the future, do not yet furnish us with the reinforcing chemicals or medications which will change an individual from one with an inherently low defense to one with an adequate defense. Our interpretation of the application of these principles will be given in succeeding chapters.

Our studies of the nature and extent of the reinforcement of the defensive blood *in vitro*, bring out many points of important information. Some individuals react in accordance with what might be anticipated, while others do not, for they may look comparatively well and strong and, upon examination, prove to have a low factor of safety. A striking illustration of low defense, which, however, I had anticipated, is that of a woman suffering from recurring attacks of rheumatism and iritis, with a general bacteremia, the organism having been recovered from her blood on many occasions. When this patient's blood was tested for its capacity to kill organisms, it was found to be very low; but the most striking feature was that the use of dead organisms placed in this patient's blood *in vitro* for even thirty minutes, almost completely failed to call forth the secondary response. Even the placing of large numbers of dead organisms failed to increase the efficiency of her blood.

Another striking illustration is the following, which is shown in Figure 254: Case No. 1417.—This patient was suffering from osteomyelitis. He had lost twenty-five pounds in two weeks' time. His freshly defibrinated blood had its maximum bactericidal capacity without the addition of dead bacteria. The

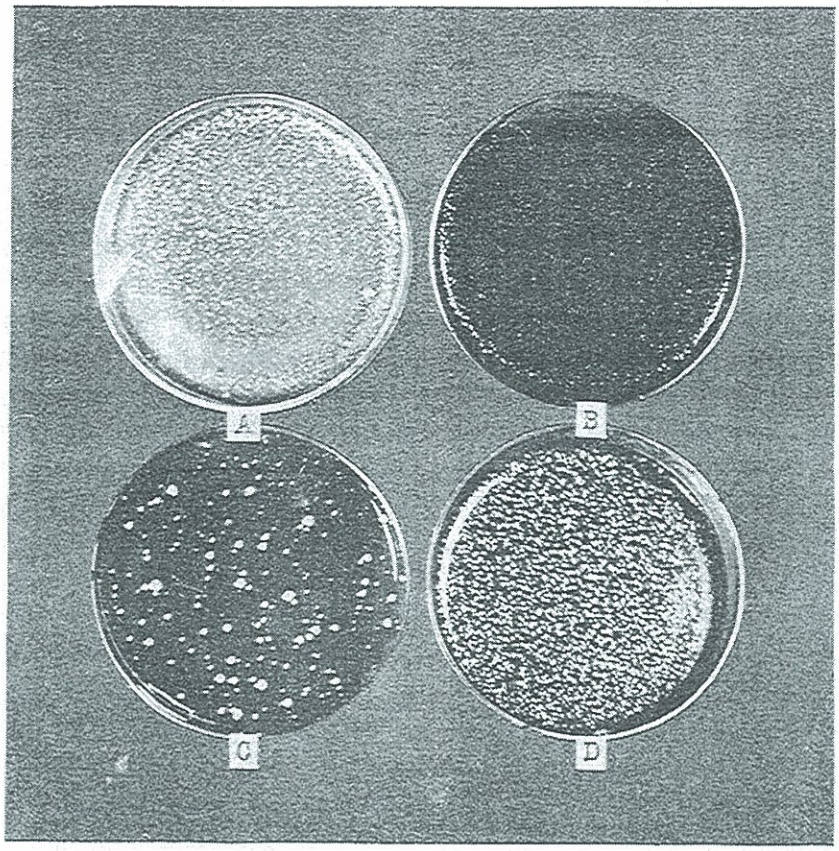


FIGURE 254. A TEST FOR BACTERICIDAL CAPACITY OF BLOOD OF A PATIENT WITH OSTEOMYELITIS. A, ONE THOUSAND LIVE ORGANISMS; B, ORGANISMS IN BLOOD FOR TEN MINUTES, NEARLY ALL DEVITALIZED; C, VACCINATION OF BLOOD WITH ONE HUNDRED DEAD, REDUCED EFFICIENCY; AND D, VACCINATED WITH ONE THOUSAND DEAD, DESTROYED DEFENSE.

addition of one hundred of these per cubic centimeter distinctly decreased its efficiency, and the addition of one thousand dead organisms almost paralyzed its bactericidal property. This patient was being stimulated to the limit of the capacity of his blood to react. The building up of his defense, as indicated by a chemical analysis of his blood, quickly reversed the trend of the battle and he gained twelve and one-half pounds in eight days' time. His case is studied in the chapter on Acid-Alkali Balance.

In our vaccines, we have found that in accordance with the suggestion of Douglas[25] that residual vaccines have in many instances apparently distinct advantage over those made in the usual way. Later work by Dreyer[26] has carried the previous

25 See bibliography.
26 See bibliography.

work of Douglas farther, and has shown that the quality of acid fastness and Gram-positive reaction obtains in organisms because of the presence in their bodies of a fatty substance probably constituting a capsule, which lipoid substance is an armor for the unit bacterium against the chemicals furnished by the host in attacking these bacteria. This substance also acts as a retaining membrane to prevent the toxic substance leaving the organism, which becomes the antigen for calling forth the antibody that is constructed by the host. If, then, such organisms be used for vaccines, their potency is very low because of this encapsulation and retention. The subjecting of these organisms to a process of extraction of these lipoidal substances, removes the defensive mechanism from the organisms, and the vaccine made from this residuum has, as we have shown in other chapters, a very marked increase in efficiency. This holds promise, with higher development and perfection, of becoming a means for the benefiting of many individuals for whom vaccines have heretofore been unavailing. It is a matter of importance in looking over our records that the individuals for whom our vaccines have been less helpful, have had as their infecting organism, a Gram-positive strain. Such a case is the one referred to in the preceding paragraphs of this chapter, with the recurring bacteremia, also discussed in the chapter on Circulatory System.

One of Nature's chief mechanisms in dealing with bacterial invasion has been shown to be a process of digestion by means of ferments probably supplied for the blood by the leucocytes. When organisms carry a large enough percentage of lipoid substances, they seem to be able to resist the action of these digestive ferments. This digestion process seems to be necessary for the liberation of the antigen, which, by its presence, will call forth the development of antibody suitable for its neutralization; and since it is the specific antigen of the organisms involved, or sufficiently similar to call forth this special ferment, that antigen is more or less specific for the organism involved. If, then, as has been shown by Dreyer and Douglas, the organism is predigested,

for which purpose they use trypsin, the product so prepared is relatively very much more efficacious in stimulating the defense of the host. We have here, then, a means for greatly improving the efficiency of autogenous vaccines. The practical application of this is illustrated in the chapters on clinical applications.

SUMMARY AND CONCLUSIONS.

We would, accordingly, summarize:

1. The blood of individuals may be reinforced by the use of vaccines, and the type of vaccine, which will be helpful, can be determined in advance by studies of the blood *in vitro*.

2. Vaccines made from organisms from which the lipoids have been extracted not only are freer from the toxic substance which produces the undesirable reactions in the patient, but have the antigen set free and therefore available for calling forth the antibody within the body of the host.

3. Vaccines containing predigested organisms, from which the lipoid substances have been extracted, have qualities which enable them to stimulate the defensive mechanisms of the host, not obtained from vaccines made from organisms without these treatments.

In some individuals a low defense may be materially strengthened by the use of vaccines and also by the use of all available means for stimulating metabolism and increasing a supply of essential nutritional factors.

CHAPTER XLIII.

CALCIUM AND ACID-ALKALI BALANCE.

PROBLEM: What is the role of calcium in the maintenance of the acid-alkali balance of the blood, other body fluids, and tissues?

EXERIMENTAL AND DISCUSSION.

Calcium enters into the structure of most of the tissues of the body, being the chief constituent of the skeleton. This, however, is not its most important role, since every form of life, from the unicellular protozoa to the multicellular vertebrate forms, is dependent upon the presence of calcium ions for metabolism and function. Similarly, every cell of the body and of every plant is dependent upon calcium ions in both its cytoplasm and the fluids surrounding it.

The present current interpretations of dental pathology are filled with paradoxes, many, if not most, of which are directly or indirectly related to calcium. But these paradoxes have not been readily cleared up by the work of the preceding chapters, for, indeed, many new ones have, apparently, been added, such, for example, as the following: Why do we have the wasting of bone, as in periodontoclasia, and apical absorption present in those individuals who have high ionic calcium, for we should expect that they would be the ones that could furnish ionic calcium for deposition in the bone; and, conversely, why do we find condensing osteitis and lack of absorption in the presence of an irritant in those individuals who have a low ionic calcium; for, if any individuals could surely ill afford to deposit bone in excess, it would be those having an already depleted ionic calcium of the blood?

What could be a more simple and satisfactory explanation for rheumatism and deforming arthritis than one providing that an abnormally high ionic calcium of the blood produces, in the presence of an inflammatory irritation, a deposition in the inflamed tissue; and, conversely, that in the presence of an inflammation due to an infective process, an abnormally low ionic calcium would cause a removal from the bone of part of its struc-

ture? The above would be a very convenient hypothesis, since in the majority of instances of deforming arthritis in the acute processes the individual has a lower than normal ionic calcium of the blood. That such a line of reasoning is not based on fact is demonstrated in many ways, one of which is that in certain types of arthritis—namely, the degenerative type—as has been shown, the ionic calcium of the blood is higher than normal, and yet to the casual observer, both types would present symptoms that would seem to be similar and would frequently be classified as identical. It, therefore, cannot be true that the ionic calcium is in itself, by its presence or absence, the causative factor. When, however, we analyze these types of arthritis, we note that with the form which is accompanied by a higher than normal ionic calcium, there is a tendency to radiolucency of the bones, with distinct softening and wastage of the calcium; and, conversely, the proliferative type of arthritis, which is accompanied by the lower than normal ionic calcium, tends to have condensation of the bone. We have, then, in these two relationships comparable conditions to those which obtained in periodontoclasia, periapical rarefying osteitis, and osteomyelitis on one hand, and the absence of periodontoclasia, the absence of apical absorption, and tendency to condensing osteitis on the other hand.

It is apparent, then, that our calcium is playing a fundamental role and our fundamental problem is to determine what that role may be. If we return to researches that I have reported on periodontoclasia, alveolitis, rarefying osteitis, etc., we will readily see that the processes which result in the tearing down of alveolar bone have direct relationship to the presence of an irritant, but not only an irritant, an irritant plus toxic product from bacterial invasion. It is not the presence alone of either, however, the irritant or the bacterial infection, that is fundamentally and exclusively the etiological factor in periodontoclasia, for if the irritant be permitted to remain and bacterial growth be reduced to a minimum, the process largely terminates; and, conversely, if the mechanical irritant be removed, in many cases the bacterial invasion reduces or disappears and the process ceases. I have also noted that the content of the periodontoclasia pockets becomes more alkaline as we go more deeply into the acutely infected pockets. It is quite easy to understand how the ionic calcium of the saliva can reach 7.4, since that is the concentration of the H ions of the blood and from which there can be but slight deviation in health

or disease. But it is not so easily explained how the stream can be higher than its source, for the pH of practically all periodontoclasia pockets will be at or above 7.4, and therefore above the pH of the blood of the individual in question. Again, as I have shown, sockets of extracted teeth which are making a rapid repair have a pH at or above 7.4, whereas those with a pH below that point are progressively slower in repair in proportion as the hydrogen ion concentration is depressed. It is also significant that the saliva of individuals with a tendency to periodontoclasia will be found to have a mien alkalinity above that of individuals without that tendency. A determination of the hydrogen ion concentration of the pus from flowing fistulae has revealed that it, too, is above that of the blood if the patient is making a winning fight. In our rabbits, however, in which a tooth is planted beneath the skin, the hydrogen ion concentration of the fluid about the infected tooth was found to have depressed to about 6.8 in those rabbits that were not making a winning fight, and always at or below that point at the time that the infection was causing the death of the rabbit.

Before discussing the experiments that I have set up for throwing further light on this question, I will review some of the characteristics of the blood itself. As previously stated, its hydrogen ion concentration (which is true of practically all the fluids which bathe tissue cells), remains practically constant at 7.4, and relatively large amounts of additions of either acid or alkali to blood will not considerably change it from this constant, whereas the same amounts added to water would produce a very considerable change. We are indebted to Henderson for the working out of the physicochemical bases of this phenomenon. He and others have shown this to be due to a very elaborate buffer system which is based upon the fact, that carbonic acid and other weak acids, like phosphoric, possess the remarkable quality of being able to maintain a constant reaction when there is present in the solution, which contains them, an excess of their salts. In the process of metabolism large quantities of carbonic acid are given off and combine directly with bases, such as sodium, to form sodium carbonate and bicarbonate, with the result that the balance is maintained between the ions of the carbonic acid and the sodium carbonate, with a constant reserve of sodium bicarbonate in the blood. The CO_2 is given off as gas in the lungs, leaving water, which continually and naturally takes

care of the elimination of the excess acid. In the consumption of foods and their reduction to sugars and fats, and the final oxidation of these products, there is a progressive burning of the carbon by uniting with oxygen, with the production of heat which maintains the body temperature and which leaves the body normally as CO_2 from the lungs. The proteins of the body enter into the process and may act as either acids or bases since they are amphoteric. Each protein has its own iso-electric point, which is the point of its minimum electrical conductivity and the point at which the H ions and OH ions balance. This iso-electric point need not be, and, in fact, with proteins does not correspond with the neutrality point of water, but with many proteins is far on the acid side of neutrality.

In the process of metabolism, the nitrogen of the protein passes by way of the splitting of the protein into the amino-acids through several cleavage processes and is in the normal individual eliminated from the body almost entirely as urea, an end product. In disturbed metabolism part of the nitrogen may be eliminated as ammonia. If, therefore, the food that is consumed is most efficiently utilized by the body, all its potential energy will be represented in the various physiological processes as heat production, work, growth, secretions, etc., and can only leave the body in the form of completely oxidized and therefore energy-free end products, which end products are carbonic acid gas, urea, and water.

This, however, presupposes an ideal efficiency on the part of the functioning of the body. It is, however, quite impossible for the quantity of intake of food to be so exactly controlled, or for the working mechanisms to be in such perfect condition as to provide for this ideal metabolism. If, in the utilization of the sugars, which is Nature's form of storing up the energy-producing products, there is not complete oxidation in these progressive stages, acids of larger molecular structure than carbonic acid will be formed; and since it is the only acid that will be eliminated as a gas, these others cannot be gotten rid of in so simple a form as is that acid, and they must, therefore, be neutralized. Such incomplete oxidation products are present as acetoacetic acid and butyric acid. The neutralization of these acids can only be accomplished by the use of bases which are present in the body. The most economical and available of these will be ammonia, and they will accordingly be eliminated as ammonium salts in the urine. When, however, the base ammonium is not available for this neutralization process, since it must be accomplished at

Case No.	Rabbit No.	Date	Days After 1st Injection	Alkalinity Index		Calcium Ionic		Calcium Combined	
				Injection		Injection		Injection	
				Before	After	Before	After	Before	After
1422	1217	7– 9–23		Imp. 45.70	Imp.	10.067		2.808	
		7–10–23	1		51.40		9.24		3.982
		7–11–23	2		51.30		7.627		2.840
		7–12–23	3		44.90		9.24		0.72
1422	1242	7– 9–23		Int-v 43.40	Int-v	8.00		2.067	
		7–10–23	1		48.40		8.128		1.112
		7–11–23	2		52.30		7.354		0.984
		7–12–23	3		50.48		7.658		1.598
		7–13–23	4		54.20		8.012		1.885
		7–16–23	7		49.13		8.857		1.728
1317	1247	7–17–23		Imp. 38.10	Imp.	8.714		2.714	
		7–17–23	½		39.10		8.714		3.894
		7–18–23	1		37.12		8.671		2.910
		7–20–23	3		44.22		9.600		2.400
		7–24–23	7		44.44		9.440		4.340
1414	1230	6–12–23		Int-v 37.85	Int-v	9.045		0.585	
		6–15–23	3				9.24		2.965
		6–16–23	4		52.40				
		7–30–23	48		27.46				
1414	1232	6–12–23		Int-v 44.25	Int-v	9.72		3.242	
		6–14–23	2				8.313		1.567
		6–16–23	4		54.45		7.727		
		6–18–23	6				8.016		2.919
		6–28–23	16		42.31				
1409	1248	7–19–23		Imp. 38.72	Imp.	10.17		1.578	
		7–20–23	1		36.88		10.60		0.534
		7–24–23	5		44.10		9.24		1.160
1409	1250	7–19–23		Imp. 32.68	Imp.	9.45		1.096	
		7–20–23	1		36.88		9.40		0.520
		7–24–23	5		44.04		9.04		2.96
1414	1234	6–12–23		Int-v 37.40	Int-v	9.45		0.180	
		7– 3–23	21		26.10				
1426	1251	7–20–23		Imp. 39.90	Imp.	8.96		0.20	
		7–26–23	6		45.90		9.26		1.085
		7–26–23	6		24.47				
1414	1235	6–12–23		Int-v 43.00	Int-v	9.640		0.320	
		7–30–23	48		30.05				
1424	1252	7–23–23		Imp. 40.88	Imp.	11.134		1.474	
		7–26–23	3		40.80		10.82		1.321
1424	1255	7–24–23		Int-v 40.00	Int-v	9.16		0.43	
		7–27–23	3		40.42		9.04		0.80
		8– 1–23	6		39.50		9.321		1.241
1426	1249	7–20–23		Imp. 38.18	Imp.	9.40		0.44	
		7–26–23	6		40.90		9.56		0.985
		7–28–23	8		36.14				
Sick Rabbit from Stock					26.40				

Imp.—Implantation
Int-v—Intravenous

FIGURE 255.

any price, the body must use such other bases as are available for its accomplishment. A continual supply of such an abnormal acid in the blood, requiring immediate and complete neutralization, since the hydrogen ion concentration of the blood will always be maintained at 7.4, must result in a depletion of those chemicals which are held in reserve in the blood for the purpose of neutralizing such abnormal acid formations. The neutralizing value of the reserve system of buffers in any blood can be determined by chemical processes. One of these is to take some of the blood serum, never allowing it to be exposed to carbonic acid gas at any moment from the time it is drawn until the determinations are made, and determine the amount of carbon dioxide that will be neutralized by it before its pH will be changed. As this method is very exacting, simpler titration methods have been perfected which give very constant results, and we have used this latter method in these studies, particularly the method of Greenwald[27].

We have, accordingly, made quite a large series of determinations to ascertain the relationships which exist between depleted buffer systems and the various normal and pathological states in which we have found our patients. I have shown in previous chapters, and particularly in Chapter 20 on the Chemical Changes in the Blood, Produced by Dental Infections, that there is a marked tendency for patients with periodontoclasia (which we will now think of as a group characteristic and as representing a constitutional state,) to develop diabetes. I have also shown in the extensive table of Figure 131 of Chapter 20, that there is a marked tendency to the development of a decrease in the alkali reserve of these patients. This has suggested a careful study to determine to what extent dental infections enter into the disturbing of the mechanisms of control for these various balances and the production of acid substances, and, particularly, to determine to what extent the calcium of the body takes part in the maintenance of the normal hydrogen ion concentration of the blood by its use in the neutralization of pathological acidities.

As one means for determining this, we have made morphological and chemical analyses of the bloods of rabbits before and after inoculating them with dental cultures or the placing of an infected tooth beneath the skin, and also when subjecting them to the filtered toxins from extracted teeth. Some of these results are shown in Figure 255. One of the important indica-

27 See bibliography.

tions is shown in the column in Alkalinity Index, in which it will be seen that rabbits starting with a normal alkali reserve—namely, an alkalinity index from 38 to 45—after being injected with a culture from an infected tooth or having one planted beneath the skin, had as one of their first effects a boosting of the alkalinity index to well above normal, which seems to be an important part of Nature's defensive reaction. When, however, these animals have become sufficiently involved to tax the defensive mechanism, this alkalinity index falls rapidly to and below normal and continues falling until they approach death. When we compare the alkalinity index column with the ionic calcium column, we find that similarly there is some tendency for the ionic calcium to go up slightly immediately following the invasion, and that as the ionic calcium goes down (which it practically always does) with the progressive overwhelming of the animal, there is a corresponding loss of alkali reserve. In other words, these animals have had established in their bodies a state of acidosis as a result of their heroic, and we should say effective, reaction in the combat against this infection.

When we compare these data with the results disclosed in the chart in Figure 131 of Chapter 20, we find that the patients suffering from severe and continued infective processes frequently, if not generally, had reductions and some very marked reductions in the alkali reserve. Case No. 1311 was reduced to 23.3. When we apply this to a similar fight against an acute dental infection in our patients, we find a similar process in progress. Case No. 1417 had an acute osteomyelitis following the extraction of an abscessed central incisor. The roentgenographic view of the condition is shown in Figure 256, and it will be noted that the necrosis had extended to the first molar, involving the lateral cuspid and both bicuspids so severely that the second bicuspid had almost completely lost its attachment. In this case it will be seen that his alkali reserve was reduced to 26.6, nearly to half its normal. In other words, he was in a state of distinct acidosis. His ionic calcium was reduced, but most important, his pathologically combined ionic calcium was up to 3.35, a very unusually high reading. The treatment of his case consisted in placing him on bicarbonate of soda, to furnish to his blood a cheaper base with which to neutralize the pathological acids and relieve it of the overload which was being paid for partly in calcium. This man had lost twenty-five pounds in eleven days. He was also placed on a liberal intake of cal-

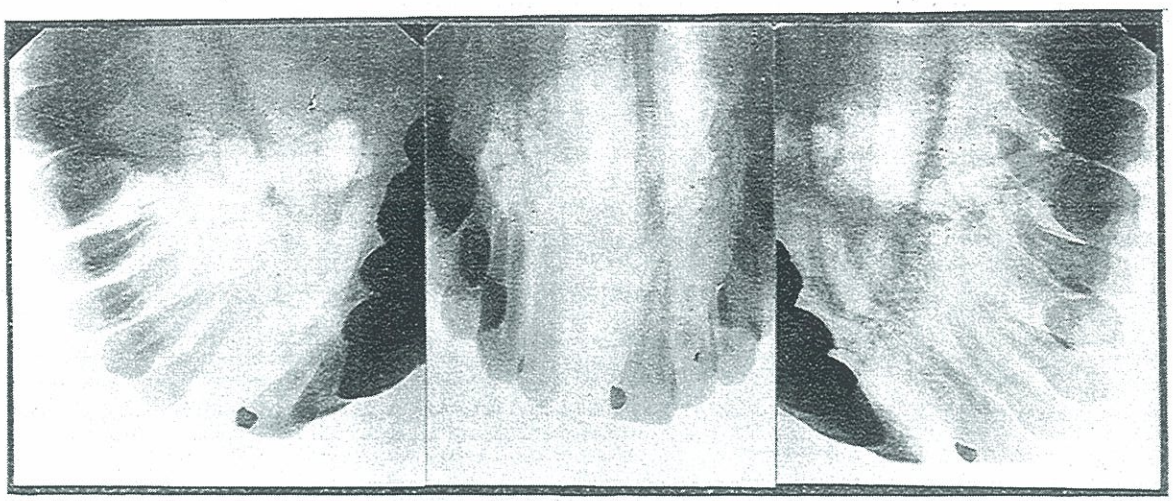


FIGURE 256. MAXILLARY OSTEOMYELITIS FOLLOWING APICAL ABSCESS.

RELATION OF CALCIUM TO ALKALINITY INDEX			
Day of Study	Ionic Calcium	Combined Calcium	Alkalinity Index
1	9.786	3.350	
3	9.785	2.857	26.60
4	10.534	1.136	25.00
7	9.045	1.235	34.70
15	9.84	1.336	30.15
23	10.935	1.405	34.68
29	10.142	1.422	30.16
36	10.314	.964	32.40
65	10.256	1.078	**41.36**

FIGURE 257.

This patient lost twenty-five pounds in eleven days during the activity of this case of osteomyelitis, and under treatment regained twenty-one pounds in a few weeks. Note that his alkalinity index progressed from the low point of 25 to 41, approximately normal.

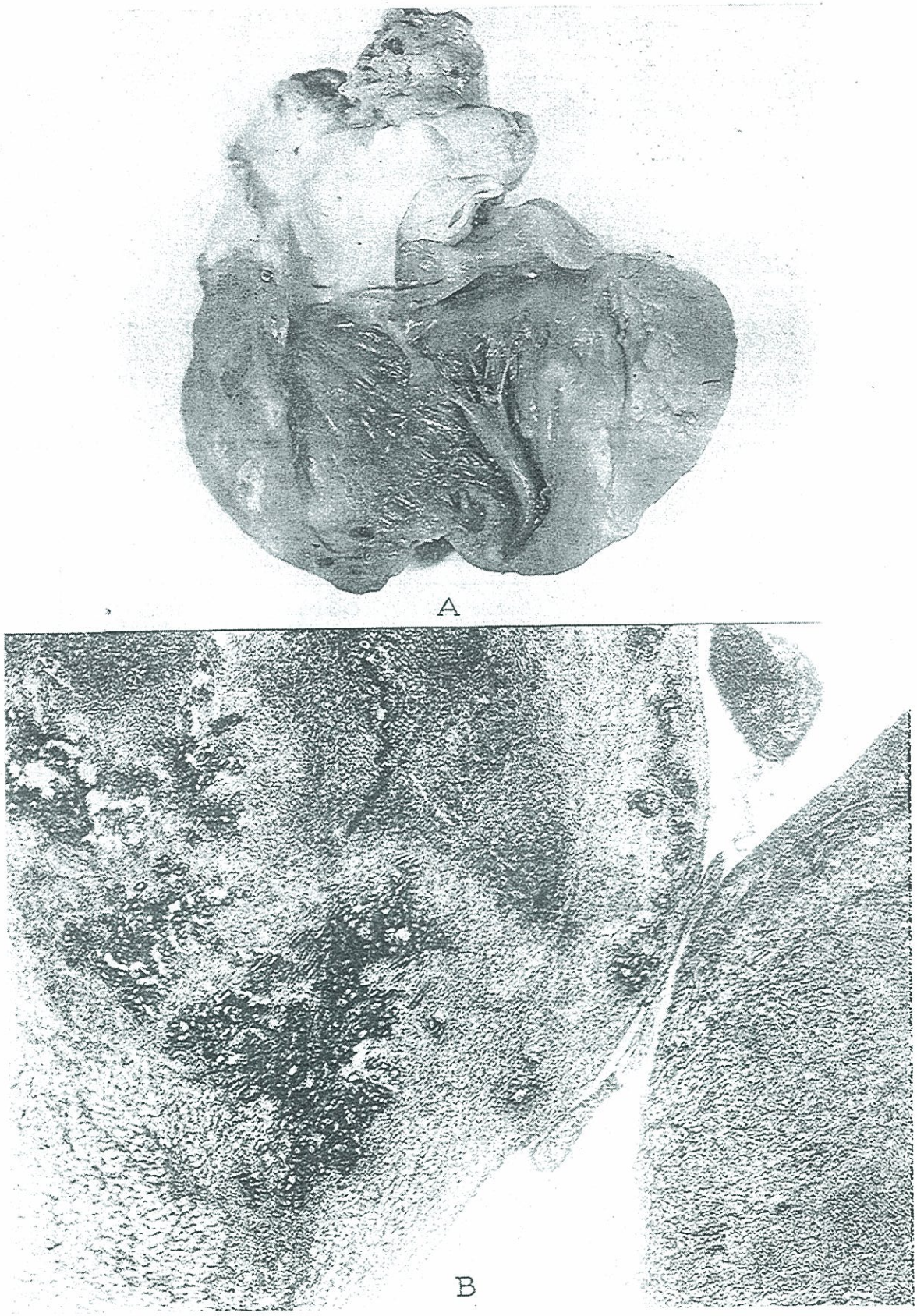


FIGURE 258. HEART OF A RABBIT WITH ENDOCARDITIS AND MYOCARDITIS; A, GROSS APPEARANCE; B, APPEARANC OF SECTION OF HEART MUSCLE WITH MULTIPLE DEGENERATIVE AND NECROTIC PROCESSES.

cium in the form of milk and calcium lactate and parathyroid to assist in the metabolism of the calcium. Results were most striking. His alkali reserve progressed rapidly toward normal, his lassitude and nervousness quite rapidly disappeared, the advancement of necrosis immediately ceased, and he gained thirteen and one-half pounds in about ten days. The relation of his ionic calcium and the pathologically combined calcium to the fluctuations in alkalinity index are shown in Figure 257. Note that, in general, as his alkalinity index went up, his ionic calcium increased and his pathologically combined calcium decreased. The condition that obtained was probably somewhat as follows: With the increase of his alkalinity index he was better able to fight the infection; with the decrease of the infection there was less toxic substance to combine with the ionic calcium to produce a pathologically combined calcium.

As a further means of study of this problem a rabbit (No. 1234) was inoculated with a culture from a patient suffering from neuritis, nervous breakdown, and heart involvement, and in twenty-one days the rabbit was chloroformed for study. One of the knees had developed a purulent arthritis and the heart had developed two major lesions, one a myocarditis with fibrosis, and the other granulation on the valve cusp, shown in Figure 258. While this rabbit was losing in weight, it was apparently not near death and yet its alkali reserve of the blood had been reduced to 25.

When we consider some of the clinical data regarding arthritic patients, we get a suggestion at once that this may be one of the important explanations for our inability to make progress with the ordinary method of treatment. This is illustrated in Case No. 1311, in which the alkali reserve was down to 23.3, and in which the ionic calcium was depressed. Under forced nutrition with milk, he was able to bring his ionic calcium up temporarily, but it did not tend to remain up without the continued pressure. The elimination of the dental infections, which were undoubtedly an important contributing factor in the development of this condition, had not been sufficient. Placing this patient on a vigorous treatment of bicarbonate as a means of testing to see whether his marked acidosis could be alleviated, if not materially improved, changed his alkali reserve to 36 in ten days' time. If our interpretation of his condition is correct, this procedure has made possible the neutralizing of abnormal acids with the artificially supplied base, sodium bicarbonate, and thereby relieving the system of the expensive process of neutralizing it with its most

available base, a calcium compound. Whether or not this is the correct interpretation, his marked improvement indicates that the metabolic processes were directly affected.

It is impossible, as yet, to explain the role of the accessory food factors and of toxic substances in the disturbances of metabolism and catabolism. It is probable that the development of acidosis in connection with scurvy and beriberi have to do with an aberrant metabolism of carbohydrate in the absence of the particular vitamin responsible by its absence for those conditions. Hamilton[28] has shown the minimum amount of calcium required per day to neutralize the products of incomplete oxidation to be 200 mgs. for an infant. If we will put this on a per kilo basis and assume that the adult requires a proportionate amount, it will readily be seen that a gram or more of calcium may be required per day. Sherman has shown a minimum daily need of the normal adult to be about six-tenths of a gram. If, however, an individual is suffering from an acidosis for which his body has not been able to make an adjustment by the establishing of a compensated acidosis, such as the neutralizing of the acid products with a base the body can spare, the demand for such expensive bases as calcium may become very great, and the amount required may be much more than the minimum above estimated. In health the sources of calcium will be mainly from the blood stream, which reservoir will be constantly replenished with food, provided that not only the laws of supply and demand shall balance, but provided the mechanisms which control calcium metabolism are in such adjustment that the balance may be and is, ordinarily, maintained. The mechanisms of control of calcium metabolism are as yet but little understood and of necessity must be very complicated. If we will take as an illustration the infinitely small amount of the activating substance that must be present to make possible the utilization for metabolic processes of the sugar of the blood, and which product is manufactured by the islets of Langerhans of the pancreas, the quantity is so amazingly small that it is almost beyond conception. To illustrate:

If the relatively concentrated product that is secured by the successive purifications of insulin is injected into a normal rabbit, a one four-thousandth of a gram is sufficient to reduce the normal sugar of the rabbit's blood from about 100 mgs. per 100 cc., to or below 40 mgs., by a process which is probably one of metabolism of the sugar, and the rabbit will go into convulsions which will

28 See bibliography.

end in death. If, however, there be injected into the rabbit's circulation a small quantity of sugar, it is almost instantly made normal.

In the pathological state of diabetes it is the inability of the body to metabolize sugar which it makes from the carbohydrates, due to the absence of this chemical. When we realize, then, that so simple a substance as sugar, Nature's principal fuel within the body, is not available except with the aid of insulin furnished by the pancreas, we see how easily it might be that even calcium metabolism may similarly be dependent upon some such delicately balanced hormone or vitamin. In the chapter on Glands of Internal Secretion, I have discussed the role of the parathyroids in this relation. If, then, we will undertake to visualize what seems to be one of the considerations in connection with calcium metabolism, it might be presented as follows:

The heat is necessary in the cold winter to keep the house warm. The fuel of choice and that we may plan to burn, may be coal. If we cannot get coal to unite with the oxygen for combustion to make the necessary heat, we may utilize wood. This wood may come from the wood yard, a base of supplies for firewood. If, however, that base gives out, the furniture of the house may be burned. Even this may not endanger life; but when the furniture is almost burned, it may be necessary to take off some of the doors and burn them for the heat of combustion for the protection of life. But the burning up of the doors and floors of the house destroys the house. It cannot function without them.

If, then, we will think of the skeleton of the body as a storehouse for calcium, just as the dwelling is a storehouse for wood, not for the purpose of having it available for fire but as the framework of the edifice, under normal conditions Nature does not require to draw upon the framework of the dwelling—namely, the skeleton—for a base with which to neutralize invading acids, the products largely of incomplete oxidation and often in part resulting from overwhelming the body with unnecessary and undesirable foods. If these substances are not oxidized and neutralized, they may accumulate in the body. If they are oxidized at the expense of fundamental bases, such as calcium, because no other product is made available by the system, the first disturbance will express itself probably in the circulating ionic calcium of the blood. There is a limit at which the body will permit this source to be overdrawn. When that limit is reached, the calcium

must be taken from the framework—namely, the skeleton—in order to pay the bills. If this process is associated with a balanced mechanism that is very sensitive to the maintenance of a compensated acidosis—that is, a constitution that sees to it that all bills are paid promptly—the individual will have the capacity for a high defense until that time comes when the available supply is not adequate, and quite unexpectedly and all too frequently we see those individuals developing some of the many types of acidosis, one of which is associated with diabetes. This capacity for paying the bills promptly not only makes the individual relatively safe against infections and invasions during the period of his ample defense, but means that in any local tissue where the body mechanisms cannot maintain this neutralization, the bills will be paid from the local storage; and if this process is part of the warfare resulting from a bacterial invasion which has developed about a mechanical irritant, such as an impinging gold crown, an irritating margin of a filling, of a food pack between the teeth, that warfare against the local toxic substance will be consummated at any cost, a part of which is the sacrificing of the alveolar bone and hence alveolitis, or periodontoclasia or pyorrhea alveolaris. If the warfare is at a root apex instead of a gingival margin, the bills will be paid in the same coin. We therefore see, if this is a part of the process, why it is that either the removal of the irritant or the removal of the toxic invading process, will cure the pyorrhea so-called. We also see why the individual who does not make this type of reaction, who does not have the capacity to pay the bill at any price, does not have this type of local expression. If, however, this individual's defense is not normally high against streptococcal infection, and he has developed a focus from which toxin and bacterial products are passing throughout his body, local zones of irritation will be established. If these occur in joints or in relation to hard structures, there may be either the tearing down of bone, or the deposition of bone, or both, just in accordance with the balance of these two forces expressing themselves in degeneration and proliferation.

The question of what becomes of the calcium and how a patient may be examined to see whether a sufficient quantity be present either in the body or blood stream for the various metabolic processes, is a most important one. It is, however, complicated by many difficulties. In the first place, any analysis based, for

example, on an incineration method, while giving the total calcium in the material being examined, throws no light whatever upon its availability for a particular use within the body, and this does not apply only to the calcified structures, for a blood with a high pathological quantity of combined calcium may, by an incineration method of calcium determination, show a normal or high blood calcium while in fact the available ionic calcium of the blood may be dangerously low. Nor will an examination of the various sera of the body show whether the calcium is being retained because of defective metabolism or elimination unless that same determination identifies the calcium structure present as being in the proper physical and chemical state which those conditions require. The calcium that is used up in body metabolism is eliminated in the feces as a calcium soap and may be considered as an end product and not available again for service within the body. The problem is therefore a most difficult one because of its many involvements. The details of calcium metabolism are not yet sufficiently known to establish what form the calcium actually takes in various of the metabolic processes.

SUMMARY AND CONCLUSIONS.

I would therefore summarize:

1. The researches recorded in this and the preceding chapters strongly suggest that one of the roles of calcium is defensive in the neutralization of products of incomplete oxidation, which are not normally present in the bodies of normal individuals, and which, when they do develop, should be neutralized by bases less costly to the body.

2. Dental infections tend to produce injury, either by disturbances of the mechanisms which control calcium metabolism or by the production of toxic substances which directly or indirectly cause the development of acid substances in the system, the presence of which depresses or inhibits normal processes of metabolism and catabolism.

I would, accordingly, express my conclusion as follows:

In the proper functioning of the body, the end products of metabolism are carbon dioxide, urea, and water. When metabolic functions are abnormal, resulting in the imperfect oxidation with the development of less simple acids than carbonic acid, these must be neutralized with bases taken from the body and its fluids. In the absence of an

adequate supply of these from other sources, the demand must be met by the calcium of the body, first from the circulating ionic calcium, then from the calcified tissues. This latter is the characteristic end reaction involved in periodontoclasia, or pyorrhea alveolaris. This enters into and complicates the etiology of many, if not most, of the rheumatic group disturbances studied in detail in subsequent chapters.

See bibliography references 29, 30, 31, 32, 33, 34, 35, 36, and 37.

CHAPTER XLIV.

DENTAL INFECTIONS AND TISSUE AND ORGAN DEGENERATION.

PROBLEM: To what extent and in what manner do dental infections contribute directly and indirectly to the degeneration of tissues and organs of the body and to disfunction of the same?

EXPERIMENTAL AND DISCUSSION.

In the preceding chapters we have studied many phases of the relation of dental infections to vital processes. In many of these we have compared, in a more or less quantitative way, the pathological states of patients. In Chapter 20, on Chemical Changes in the Blood Produced by Dental Infections, I have shown many instances of parallelism between the pathological states of the patients, as expressed serologically, with those produced in rabbits and rats that had been subjected to either the inoculations with dental cultures or planting of infected teeth beneath the skin. In Figure 131 of that chapter I have given approximately one hundred successive analyses of the blood, and related them to the dental pathology and systemic conditions of the patients. These reveal many instances of important associations, as, for example, a high ionic calcium of the blood with periodontoclasia, and of both high ionic calcium of the blood and periodontoclasia with hyperglycemia and glycosuria. Similarly, it was shown that with the development of extensive toxic disturbance from dental infection, patients tended to have reduction of the ionic calcium of the blood with an increase of a pathologically combined calcium of blood, which condition was practically universally produced also in experimental animals, whether they were inoculated intravenously with a strain taken from a dental source or whether a tooth was planted beneath the skin of the experimental animal.

Data were presented which seemed to demonstrate that a disturbance of carbohydrate metabolism when it exists in patients, as in diabetes mellitus, may be influenced by the removal of dental infections, and, similarly, changes in the blood sugar of

experimental animals could be produced with dental cultures, amounting to a distinct hyperglycemia. In the chapter on Glands of Internal Secretion the researches reported seemed to establish that dental infections may very definitely disturb the functioning of these various structures, especially that of the thyroid and pancreas. In the chapter on Elective Localization of Bacteria of Dental Origin, the data developed by the researches reported seem to establish, as has the work of several others, that dental infections have a direct relation to, and are important contributing factors in, the establishment of infective processes in various organs and tissues of the body. While these various studies strongly indicate that there is a distinct responsibility on the part of dental infections in the production of degenerative processes in the organs and tissues, the data presented do not make sufficiently clear the fundamental nature of the process involved. This research has therefore been undertaken to establish, if possible, more exactly the nature of these processes.

In Chapter 41, in studying the defensive mechanisms of the blood, many important new data were presented, which established in further detail the role of the leucocytes and the fact, that they are under certain conditions paralyzed by dental infections and probably by the toxins from infected teeth. In Chapter 43 we have seen how calcium may be taken from the circulation to neutralize products of incomplete oxidation in the absence of some other base less costly to the patient than the calcium. Since a freshly extracted infected tooth, when placed in defibrinated blood or blood serum, will in many instances very greatly reduce the ionic calcium of that blood and, which may accordingly be present and measurable as a pathologically combined calcium, may it not be that this toxic substance may have a direct relation to either the more gross factors involved in metabolism, or, more important, be directly related with the governing factors controlling the detailed processes of metabolism and catabolism? We might, therefore, restate our problem: What are the relations of the products of dental infections to processes of metabolism and catabolism and to the organs and tissues engaged therein?

As one method of approach to this problem I have had studies made to observe the changes in the alkalinity index, or so-called alkali reserve, of the blood. Before proceeding with this discus-

ALKALINITY INDEX OF BLOOD OF PATIENTS

Case No.	Alkalinity Index	Dental Symptoms	Systemic Symptoms
1311	**23.30**	Slight Locked Apical	Rheumatic Arthritis
1337	**39.40**	Several Locked Apical	Enlarged Cervical Glands and Lassitude
1325	**42.37**	Periodontoclasia	Rheumatism
1339	**39.50**	Locked Apical	Neuritis
410	**34.4**	Periodontoclasia	Normal
1346	**47.20**	Chronic Periodontoclasia	Normal, after illness
1409	**31.8**	Locked Apical and Periodontoclasia	Lassitude
1332	**46.0**	Slight Locked Apical	Normal
1359	**41.0**	Locked Apical	Nervousness
1363	**36.14**	Locked Apical	Rheumatism and Nervousness
1416	**38.65**	Periodontoclasia	Degenerative Arthritis
1417	**26.60**	Suppurative Necrosis	Osteomyelitis
987	**32.50**	Normal	Rheumatism and Heart
335	**32.53**	Normal	Bursitis and Lassitude
1421	**39.39**	Periodontoclasia	Near Normal
1419	**25.49**	Locked Apical	Lassitude and Hypertension
1324	**20.36**	Periodontoclasia	Osteomalacia
1425	**27.16**	Locked Apical	Nephritis
1381	**23.00**	Chronic Ulcers	Normal
1423	**34.24**	Apical and Gingival	Hyperthyroidism
1381	**32.22**	Normal	Lassitude
1417	**31.20**	Suppurative Necrosis	Osteomyelitis
1311	**33.94**	Normal	Deforming Arthritis
1427	**25.90**	Periodontoclasia	Tuberculosis
1428	**24.20**	Periodontoclasia	Tuberculosis
410	**25.30**	Chronic Periodontoclasia	Periostitis and Lassitude
425	**29.63**	Locked Apical	Digestive Trouble
2168	**23.76**	Periodontoclasia	Diabetes

FIGURE 259.

ACID-BASE RELATION TO SYMPTOMS AND TREATMENT. CASE NO. 1417

Day of Study	Ionic Calcium	Combined Calcium	Alkalinity Index	Urine pH A.M.	Urine pH P.M.	Weight	Gain	Loss	*Systemic Treatment
1	9.786	3.350				133¾			
2									Systemic Nos. 1, 2, 3
3	9.785	2.857	26.60						
4	10.534	1.136	25.00	5.52		133½		½	Continued Nos. 1, 2, No. 3, 10 grs.
7	9.045	1.235	34.70						Continued all
11						136½	2¾		Continued all
12						137¼	3½		Continued all
13						138	4¼		Continued all
15	9.84	1.336	30.15	5.39		138¾	5		Continued all
16				6.59		138		¾	Continued all
18				4.98		140¼	6½		All discontinued by me.
20				5.14	4.99	140		¼	All discontinued by me
21				4.99	5.14				All discontinued by me
22				3.96	4.24	139		1	All discontinued by me
23	10.935	1.405	34.68	4.18	4.87	141	7¼		Resumed No. 1, 2 No. 3, 15 grs.
25				5.42	6.62	140		1	Continued All
27				5.39	6.53	140	6¼		Continued All
29	10.142	1.422	30.16	4.28	4.51	141	7¼		Patient neglected No. 3.
30				6.03	6.84				Resumed All
31				6.65	6.95	142½	8¾		Continued All
32				6.76	7.23	143¼	9½		Continued All
33				6.23	7.75				Continued All
34				7.33	7.84				Reduced No. 3 to 5 grs.
36	10.314	0.964	32.40	6.96	6.98	145½	11¾		Reduced No. 3 to 5 grs.
65	10.256	1.078	41.36	5.63	5.97	145	11½		Discontinued all

*Systemic Treatments.
No. 1—Parathyroid 0.1 grain daily.
No. 2—Calcium Lactate 5 grains 3 times daily.
No. 3—Bicarbonate of Soda 5 grains half hourly.

FIGURE 260.

sion it is desirable to call attention to the fact, that there is strong opposition to the use of the term "Alkaline Reserve" because the term presupposes that in addition to the alkali that is held in combination, there is a quantity stored up available for sudden demands, but which, while in storage, is taking no part in the process of metabolism. Haldane and others have shown (British Medical Journal, April 9, 1921) that in cases where the blood is abnormally alkaline, the actual alkaline reserve may be diminished, and, conversely, that it may actually be increased in cases where the blood is deficient in alkalinity. He shows how that in actual fact the whole of the normal alkaline reserve is required to balance the carbonic acid normally present. Macleod has shown how in many cases (Physiology and Biochemistry in Modern Medicine) that there may be a compensated acidosis or a compensated alkalosis. In our studies of patients with degenerative processes of the various rheumatic group lesion types we have found a great divergence in the alkalinity index of the blood. In Figure 259 will be seen a group of twenty-eight successive individuals, and it will be noted that the variation runs from 47.2, approximately normal, to 20.3. When, however, we compare the physical condition of these various patients with this alkalinity index, we find immediately that the individuals in the most serious condition have the lowest alkalinity indices; whereas, those normal, or approximately normal, have an approximately normal index.

Case No. 1417 has had an osteomyelitis which has been checked very quickly by the administration of sodium bicarbonate, together with the administration of parathyroid, one-tenth grain daily, and calcium lactate, fifteen grains three times a day; and this patient who lost twenty-five pounds in a couple of weeks' time during the suppurative process, gained eighteen and a half of it back in about two weeks' time after being placed on this treatment. Notwithstanding the fact, that he was receiving fifteen grains of bicarbonate every half hour during the day, at least was supposed to get this amount, his urine did not become alkaline. To check the relationship of these conditions more exactly to the neutralization of acid products within his system, the bicarbonate and all treatment was stopped, with the result that he lost in weight, the suppurative process increased, and his urine quickly became strongly acid. He was placed back on the bicarbonate, parathyroid, and calcium treatment, and in twenty-four hours there was a distinct improvement which was marked

in forty-eight hours. When asked what the particular differences were that he could recognize in his feelings, he said that when he was taking the medicine he felt rested when it was time to get up and wakened up fully awake; whereas, when he was not taking the medicine, he did not feel rested from his sleep.

In Figure 260 we see in parallel columns the ionic calcium, the combined calcium, the alkalinity index, the treatment, and change of weight of this patient. It will, accordingly, be seen that we have here a very strong indication that a disturbance of the acid-base balance is an important factor in his pathological state. When we review the history of his case, we find that he had a neglected gingival infection. An acutely abscessed tooth was extracted. The socket became infected from his gingival infection, for the spirochetes were found deep in the necrotic bone though his chief infection was streptococcal. His acute apical infection lowered his general defense so suddenly and severely that he apparently became a prey to the spirochetal and mixed infection of the gingivæ, which still more rapidly overwhelmed him. Fig. 260 also shows the pH of the urine.

In order further to check the effect of dental infection, I have had placed infected teeth beneath the skins of rabbits in order that we might compare the morphological changes in the blood, the ionic calcium, combined calcium, and alkalinity index. A group of these are shown in Figure 261. In rabbit 1234 it will be noted that at the time of death the polymorphonuclears had dropped to the very low count of 13.3 and the small lymphocytes had increased to 81.6. The ionic calcium had fallen from 9.4 to 7; the pathologically combined had increased from 0.18 to 2.83, and at death was at 1.52. The alkalinity index of this rabbit was 37.4, slightly below normal, when the experiment was started, and decreased to 26.1. This rabbit was chloroformed twenty-one days after being inoculated with the dental culture from a patient suffering from heart involvement and neuritis, and this rabbit had endocarditis, myocarditis, and joint involvement. Rabbit 1217 died in three days after the planting of a tooth, and it will be seen that the chief effect was an increase of the alkalinity index. This will be discussed later. Its polymorphonuclears decreased and its small lymphocytes increased. The ionic calcium dropped from 10 to 7.6. We have, therefore, in the second rabbit, a quite different reaction from that in 1234. When we take a number of terminal readings on rabbits with

Case No.	Rabbit No.	Days After	Alkalinity Index		Calcium Ionic		Calcium Combined		Weight			Days Lived	Blood Count			Remarks
			Before	After	Before	After	Before	After	Per Day	% Loss	% Gain		Whites	Polys	Small	
A1422	1217	Imp.	45.7		10.0		2.80		1419				9,600	37.5	50.0	Emaciation, congestion of heart.
		1		51.4		9.24		3.98	1387				6,800	45.0	50.0	
		2		51.3		7.62		2.84	1325				7,600	31.5	62.9	
		3		44.9		9.24		0.72	1289	9		3				
A1414	1234	Intv.	37.4		9.45		0.18		1219				7,400	13.3	81.6	Chloroformed. Endocarditis and Myocarditis, right knee arthritic.
		21		26.1					1197	2		21				
A1426	1251	Imp.	39.9		8.96		0.20		995				10,800	46.6	44.5	Emaciation, hyperemia, subcutaneous abscess.
		6		45.9		9.26		1.085	959				7,200	32.5	56.5	
		6		24.4					862	13		6	4,600	36.8	52.6	
B1317	1247	Imp.	38.1		8.71		2.71		1165				14,200	28.3	62.3	General condition good. Locally large hard swelling at site of implantation.
				39.1		8.71		3.89	1146				10,500	21.0	65.0	
		1		37.1		8.67		2.91	1176		1		9,800	28.0	63.1	
		3		44.2		9.60		2.40	1162				18,800	63.6	31.8	
		7		44.4		9.44		4.34	1129	3			18,300			
B1414	1232	Intv.	44.2		9.72		3.34		1145							Paralysis, and emaciation. Very alert.
		2				8.31		1.56								
		4		54.4		7.72			1072				12,900	39.3	49.1	
		6				8.01		2.91	1079				9,200	37.6	56.7	
		16		42.3					1015	11			14,500	43.4	45.3	
B1409	1248	Imp.	38.7		10.17		1.57		1322				17,200	35.0	34.7	Slightly emaciated. Small swelling. Very alert.
		1		36.8		10.6		0.53	1298				12,200	50.4	43.3	
		5		44.1		9.24		1.16	1279	3			16,000			
B1409	1250	Imp.	32.6		9.45		1.09		1302				12,800	36.5	56.0	No abnormal developments.
		1		36.8		9.40		0.52	1280							
		5		44.0		9.04		2.96	1263	2			4,000			
B1414	1235	Intv.	43.0		9.64		0.32		1335				18,000	58.3	34.6	General condition good.
		48		30.0					1437		17					
C1414	1230	Intv.	37.8		9.04		0.58		1324				9,100	30.0	60.0	Slightly emaciated, otherwise O. K.
		3				9.24		2.96	1285				15,000	27.0	69.0	
		4		52.4					1233							
		48		27.4					1490		11		14,200	37.7	56.6	
C1424	1252	Imp.	40.8		11.13		1.47		1959				14,200	26.3	63.1	Slightly emaciated, swelling on back.
		3		40.8		10.82		1.32	1912	2			16,400	19.5	68.0	
C1424	1255	Intv.	40.0		9.16		0.43		1254				10,700			Slightly emaciated, otherwise normal.
		3		40.4		9.04		0.80	1247	.6			17,000	70.6	20.6	

A—Killed by infection, or near death when chloroformed.
B—Making good defensive reaction.
C—Not injured by infection as yet.

FIGURE 261.

implanted teeth, we find that not infrequently the alkalinity index goes down to and below 25.

In Chapter 30, The Nature of Sensitization Reactions, I have shown the results of studies comparing the toxin of dental infections with histamine, and it was shown that there were some factors in common, one being the marked engorgement of the mesenteries, dilatation of the blood vessels of the small intestine, and one sensitized rabbit died within two minutes after receiving its infection. Further studies of this toxic substance indicated that it had some characteristics differing very distinctly from those of histamine. This suggested another approach to this problem.

On reviewing the various data of the preceding chapters, it has been disclosed that a very frequent effect of dental infections on both humans and experimental animals (when the latter had an infected tooth placed beneath the skin or were injected with a dental culture) was the production of creatin and creatinin in the blood and urine. For example, the normal quantity of creatinin in urine is given by some authorities as ranging from zero to 80 mgs. per 100 cc. of urine. In a series of thirty-three approximately successive patients it was found to vary from 40 to 260; and when we study the patients we find one, for example, with 200 mgs. was ill in our ward with a very bad heart involvement, which rapidly cleared up after the removal of her dental infections. Another, 240, had a near nervous breakdown. Studies that have been made of various expressions of acidosis have demonstrated the increase in creatinin with the acidosis.

Noel Paton[23] has shown that creatin may be regarded as a substituted guanidin; and Watanabe[24] has shown that the injection of guanidin directly into rabbits produces an acidosis with development of albuminuria and casts. I have, accordingly, undertaken to establish somewhat of the relationship between the toxic substance produced in infected teeth and guanidin. One of the methods of approach has been to defibrinate freshly drawn rabbits' blood and to add to one tube of it 200 mgs. of a 5 per cent solution of guanidin carbonate to 2 cc. of blood. A second tube was similar except the use of guanidin hydrochloride instead of the carbonate. In a third tube of the blood, pieces of a crushed infected tooth were placed and a fourth tube was used as control. The control tube showed an alkalinity index of 40.6.

23 See bibliography.
24 See bibliography.

The tube with the guanidin carbonate showed an alkalinity index of 51.4, the guanidin hydrochloride 24.2, and the blood with the pieces of crushed tooth 68.2. It will be noted that, whereas the ionic calcium of the normal blood was 11.1, when the crushed tooth was placed in it, its ionic calcium decreased to 8.2. Since the quantity of alkali which was introduced with a small piece of tooth was so insignificantly small that it could not possibly account for, from a chemical standpoint, the marked increase in base in the blood, from whence and how did it attain that state, for the change in the capacity of the blood plasma to absorb 40.6 grams of carbonic acid per 100 cc., increased to 68? This immediately suggested that the reservoir of the blood had possibly been drawn upon.

In Chapter 43 I have briefly reviewed the process of development of incompletely oxidized products which are acid in reaction and which must be immediately neutralized, for which purpose the body uses its most available bases, and in the absence of others seems to use the calcium. Henderson and Spiro have shown that the alkali of the blood is largely carried in the red blood cells though there is a sufficiency for the needs of the blood plasma, as bicarbonate, in it. The red blood cells are capable of taking up acid as carbonic acid increases in the body, and carry it to the lungs where it escapes as carbonic acid. The mechanism which controls this equilibrium, while probably purely a physico-chemical one, is one of the most delicate and exact of all the processes of the body. May it not be that the toxin contained in an infected tooth, which is capable in ten minutes' time so to change a few cubic centimeters of blood as to reduce the ionic calcium 10 to 50 per cent, even though the root tips only of the whole tooth are placed in the blood, with therefore no appreciable loss in weight of the tooth itself, may be able to produce these far-reaching changes in both ionic calcium and hydrogen ion concentration either by entering into combination with some of the hormone or enzyme substances or by acting as such itself?

When we review some of the outstanding effects of dental infections, we find among them a tendency of the individuals suffering from them to be underweight except in those cases of tissue infiltration with edema, where their appearance may be very deceiving. I have also shown that the placing of the filtered washings from teeth into rabbits, tends very markedly

to reduce their weight, and, perhaps, most important, starts a series of metabolic changes which go on to complete emaciation and death even though the evidence strongly indicates no living organisms were introduced. Indeed, this process has been produced with heated tooth extracts and with heated infected teeth and even with some autoclaved teeth. We seem, therefore, to be dealing with a substance which may or may not have properties in common with guanidin, which matter our studies are endeavoring to disclose, but which toxin acts directly upon the fundamental controlling mechanisms of the body. It we will think of the smallness of the quantity of insulin, one four-thousandth of a gram, which, when injected into a rabbit, will so activate the mechanisms of the body for burning up sugar as to reduce the blood sugar so rapidly and completely as to cause the death of the animal, and when we realize that without any insulin, the rabbit or human is entirely unable to metabolize sugar, we realize what infinitely small amounts of the activating substances will be required for life's processes. Let us think for a moment of the thyroid. Marine has shown that a couple of drops of iodin placed on a dog's tongue at the time of the development of a goiter, will prevent the typical development of the pathological process, and also that the administration of a few grains of potassium or sodium iodide, or iodin in any suitable form, to growing girls once or twice a year will completely protect them from the development of goiter, and that animals so suffering can be cured by these almost incalculably small quantities in proportion to their body weight. Or again when we think of the quantity of Vitamin B that is necessary for an animal to prevent the development of the typical lesions of the nervous system, we find it to be the infinitely minute quantity of one two-hundred-thousandth part of a gram per day per kilogram of weight. Or again, when we think of the quantity of toxic substance which extracted from a tooth will be sufficient to produce marasmus in a rabbit, we find it to be only a minute fraction of a milligram. We have not been able to measure it, it is so small. We are, therefore, dealing with a substance in these infected teeth which, like the activators of metabolism and the hormones controlling function, have to be dealt with and considered in terms of their effects rather than in terms of their mass. When we reflect the popular opinion regarding the quantity of dental infection necessary to produce disturbances and compare it with the facts, we find an

ample explanation for the divergence of opinion.

But there is another phase of this problem which must be considered in this connection, and that is the clinical in its relation to the removal of dental infection, for if dental toxins and dental infections have so far-reaching effects on metabolism and catabolism, we should get many important data from the study of the individuals from whom these infections have been removed. This very important phase of this problem has not been neglected, but is so voluminous as to require a separate volume approximately the size of this one, and since the data have been simultaneously developed, it is being simultaneously published. It is important, however, to state in connection with the argument of this chapter that the removal of dental infections from not a few hundred but from several thousand individuals (many of whom have had chemical and morphological studies of the blood and fluids of the body as controls for the symptomatic change) has developed a fund of information which clearly establishes that the removal of the dental infections has completely changed the symptomatology, to accomplish which, fundamental changes were produced in the metabolism and catabolism of their bodies.

If lack of space did not prevent, we could, by briefly reviewing the clinical researches that are reported in Volume Two, present many illustrations of the change of metabolic processes by the removal of dental infections, and these would relate to a great many, if not nearly all, of the important organs of the body. I will illustrate with just one case which is reported in detail in Chapter 66 on Eyes. The woman presented with marked exophthalmic goiter. Exophthalmos is a symptom that is so clearly related to the functioning of the thyroid that we can without question classify it as a controlling factor in metabolism. There are two phases of the case to be noted here especially. The first is (and we have many cases illustrating this) that there was marked improvement in the appearance and condition of her eyes in a very few days after the removal of her dental infections, and in the chapter referred to it will be seen that her protruding eyes reduced to practically normal position and size in a few weeks' time. The other important item to note is (and this is also illustrated with the photographs of the rabbits in that chapter) that several rabbits that were inoculated intravenously with the culture from her infected teeth when they were removed, developed within forty-eight hours very marked bulging exophthalmos, a

condition that has not developed in 1 per cent of 1200 rabbits inoculated with miscellaneous cultures. This seems strongly to suggest that her dental infection was directly affecting her metabolism through its effect on the thyroid, as was also evidenced by the very great improvement of her nervous and heart symptoms.

Similarly, we might review disturbances of hearts, kidneys, gall-bladder, ovaries, testicles, nervous system, digestive system, special tissues, etc., and cite case after case as part of the experimental data of this chapter. I will, accordingly, ask the readers of the second volume to keep this phase in mind—namely, the relation of the dental infection to those forces which control metabolism and catabolism.

I would, therefore, summarize as follows:

Since dental infection affects directly the ionic calcium of the blood and the acid-base balance of the blood, it is affecting two of the most fundamental factors in all of life's processes, which, if continued, will of necessity produce degenerative changes in the tissue so altered, for no change can express itself in function without a physical or physicochemical change in functioning tissue. Henderson has stated that of all the regulating mechanisms of the body, the acid-base balance is the most important and far-reaching. This is so because every process of body function is dependent directly upon hydrogen and hydroxyl ion concentration. If, then, the toxin of dental infection can influence Nature's most fundamental governing process, we find an important new light on the etiology of the degenerative diseases, and in the second volume, which is a continuation of this study from the clinical pathological standpoint, I have undertaken to interpret in the terms of the individual cases, the various processes concerned in so far as our present knowledge makes that possible. When we reflect that the various expressions of shock are primarily due to acidosis, as shown by Crile, Cannon, Wright, and others, and further that all symptoms of an acute shock may be produced in experimental animals by the introduction within their bodies of the small amount of infection and toxin in an infected tooth, and further that humans carrying dental infections for a long period develop a state which might be expressed as a low-grade and chronic shock, we get a new meaning for this type of toxic invasion. I would, therefore, present the foregoing as simply a preliminary report and stress the necessity for more

exhaustive researches on these fundamental problems.

I have endeavored to make the reports of these studies as brief as possible in order that this volume might not be too cumbersome. It has already more than doubled the dimension originally intended, which has compelled the publishing of this report in two volumes instead of one, and notwithstanding this brevity I have presented only a small fraction of the data which I have accumulated in these various studies. The presentation of a new basis of interpretation, which I shall give in the succeeding chapters of this volume, together with my interpretations of the clinical pathology, as presented in the next volume, constitute this first preliminary report. I have, however, in course of preparation, data on the practical application of these various processes with a desire to assist the members of the dental and medical professions in dental diagnosis, prognosis, and treatment, and, primarily, in the prevention of the dental lesions. Of necessity this work requires a great deal of time and the expenditure of an almost unbelievable amount of energy and, incidentally, a very large expense. The importance of the work makes all these justified, subject always to the un ontrollable limitations of resources and physical endurance. In other words, it will take many months of additional work to complete Volume Three on Dental Infections, Their Diagnosis, Prognosis, and Treatment.

Summary and Conclusions.

I will, therefore, briefly express the conclusions of this chapter as follows:

Dental infections disturb directly the acid-base balance of the blood and thereby prevent the catabolic processes which would remove from the body the products of tissue reaction, food intake, etc., as inert end products, (chiefly as urea, carbonic acid, and water). This disturbed catabolism directly and in association with other disturbing factors, results in the production within the body of acid products which are neutralized by the body with difficulty and at the expense of other vital processes. Their retention within the body injures not only the tissues involved normally in the process of their elimination, but disturbs directly the processes of metabolism and catabolism. These express themselves as disfunctions, and organ and tissue degenerations, and constitute an important factor in the morbidity and mortality of even our most advanced civilizations.

Since the hydrogen and hydroxyl ions constitute by their mutual relationships and proportions not only the mechanism of control of the acid-base factors, but by their proportion in various fluids determine the functioning qualities of various organ and tissue cells, they probably constitute the most important hormone of the body, and any forces which disturb their relation will thereby disturb the functioning of practically every cell of the body of the individual, which processes, if continued, result in structural change and disfunction and organ degeneration. Since dental infections exert so direct an influence on this fundamental hormone, they become directly the cause of extensive and destructive degenerative organ changes.

See bibliography references 38, 39, 40, 41, and 42.

CHAPTER XLV.

INTERPRETATIONS. THE LOCAL PHENOMENA OF DENTAL FOCAL INFECTION.

DISCUSSION.

Focal infection, whether dental or otherwise, resolves itself fundamentally into a warfare between two biological units, one unicellular and the other multicellular, the former a parasite on the latter. Under ordinary conditions the invader is dependent upon a defect in the cellular structure of the latter, which defect may take the form of traumatized and therefore abnormally nourished and injured tissue, or of partially poisoned tissue, the result of toxic invasion or other foreign poison. The invaded host is thereby handicapped in its warfare against the invading parasite. True, there are a great many different types of invading organisms, some generating a poison which paralyzes or kills the tissue in advance of the invading organisms, and thereby prepares the way for them. Still others live in the tissue without apparent local irritation to that tissue. They may generate exo- or endo-toxins and they may select any of the varied tissues of the body as their habitat, some even limiting their activities to the cells of the blood.

The disturbances with which we are concerned, whether of the teeth or of other tissues, but particularly the former, which produce local foci that develop toxic substances and bacteria which invade the body, are dependent pretty largely upon an organism or group of organisms having quite definite local and systemic characteristics, both from the point of their morphology and of the reactions they produce. For convenience we speak of the lesions they produce as the rheumatic group lesions, rheumatism being but one of the many disturbances. We are particularly concerned with the characteristics of the invading organism in this type of lesion, since so many of the deficiency diseases (old age diseases) are indirectly or directly influenced, and in many instances caused, by these local processes.

This entire group of researches is primarily a study of this war-

fare in its various phases. Since it is a contest between two biological units, our first problem seems clearly to establish the responsibility of each. Arguing from analogy, we saw in Chapter 2 that if we will consider this invading organism as having similar characteristics to those of the many infectious diseases with which we are so familiar, and which have been so far-reaching in their devastations, we will expect of it, when in this type of lesion, that it shall have brought into its environment the weapons which prepare it for the particular type of expression which it will later develop. If we will think of any of the biological units which we are associated with, we find that they have very limited capacity for adaptation. The beaver must have soft wood trees to gnaw and live upon, and water in which to swim. The feline kind must have animal life to live upon; and, similarly, we find species which will limit their activities to very narrow ranges throughout the entire field of life.

It is, therefore, natural that we should have expected that the organisms with which we are concerned in this special study, would have very definitely fixed qualities which would determine their elections and expressions. We found, however, in Chapter 2 that contrary to this natural expectation, which is almost universal in its acceptance, the organisms with which we are concerned in this type of pathological process do not bring with them their essential characteristics which perforce establish and predelect the characteristics of the local and systemic expression. On the contrary, the different morphological characteristics and classifications of the varieties are found in the different types of pathological expression in the order of chance, with utter disregard to the biological differentiations. We further found that while this type of lesion is produced almost entirely by a group of organisms, which we speak of as streptococci and diplococci, growing in one or the other form, and largely in accordance with the media in which they are growing, they have the remarkable property and capacity which enable them to adapt themselves to most extreme and unexpected conditions, even coming to grow luxuriantly in concentrations of poison, which completely inhibited their growth and devitalized the earlier generations which formed a part of their antecedents, before they had availed themselves of this wonderful quality of adaptation; and further we found that these non-spore-forming organisms have the capacity for taking on forms which are very similar to the spore formations, in effect, of the truly spore-forming varieties of bacterial cells.

We have, therefore, as the first important goal in the analysis of this struggle between these two biological units, that the invading organism, while infinitely the smaller, is destined to win the battle if only time enough may be granted, largely on the basis of this one quality of its marvelous ability for adaptation to its environment. We have in this wonderful quality, however, perhaps one of the greatest forces in the development of our animated life. It has been by this quality of adaptation, that those earliest unicellular forms developed into the more resistant and more adaptable multicellular forms and all the way up, for some of the writhing monsters in the warm pools where the waters dried up into mud developed their fins into legs and their gills into lungs, etc. This law of adaptation enabled these creatures through long ages of time to go out upon the hardening slime and adapt themselves to a changed environment; and, ultimately, by adaptation, the forms of life adapted to all the conditions from the torrid to the frigid zones; and even so man has grown, for archeologists show us that man made his greatest advancement out of the stone age into more efficient methods of living, partly as a result of the hardships of the ice age.

When we review results of the many hundreds of rabbit inoculations with cultures grown from infected teeth, it is a matter of profound importance and significance that almost universally all other strains are killed off in the animal's body except the diplo- and strepto-coccal forms. It is true that in a few instances staphylococci will also be isolated, but, proportionately, these cases are rare; and aside from these two, it is an exceedingly rare exception to find any other oral type of infection. In later chapters, for example, I record some spirochete systemic involvements. In our studies in Chapter 41, we found that when the lymph extracted from humans and from rabbits was inoculated with the mixed strains and varieties that grow in the human mouth, the principal strains to grow out were the diplococci, streptococci, and staphylococci. This brings us to ask why these are the facts. May it not be, and, indeed, is it not probable that again the law of adaptation has been at work, that as these organisms have grown as commensals in the mouths of all humans during the tens of thousands of years of their existence, they have come in contact with the body fluids through gingival abrasions and carious teeth until they have actually come to live in and upon modified normal tissue fluids? But the question may be asked, "Why is this not just as true of all the spirochete and bacillary forms?" The

answer to this may be that the local and systemic defense, or rather disturbed defense, produces an environment which, because of hydrogen ion concentration changes and other biological and chemical factors, these latter do not find within the range of their adaptability; nor, indeed, do we find evidence that they have nearly so great a capacity for adaptation as the diplostreptococcal and staphylococcal varieties.

We would, therefore, summarize the Local Phenomena of Dental Focal Infection as a warfare between two biological units, one unicellular with a most remarkable capacity for adaptation, the other, the host, multicellular, with normally in normal tissue a defensive capacity adequate to combat and obstruct the invasion of the former. When the defense of the host breaks at any point, the invader through its marvelous capacity for adaptation increases its attacking power and develops its defensive factors to resist the attacking mechanisms of the host. The fundamental point of break, therefore, is in the failing defense of the host, and our problem largely consists in studying the various changes of environment that may be provided by the host.

CHAPTER XLVI.

INTERPRETATIONS.
THE PHENOMENA OF LOCAL REACTION.

DISCUSSION.

In the preceding chapters we have reviewed several researches which were undertaken to verify or correct the generally accepted premises on which our interpretations are made. These studies have shown very clearly that things are not always as they seem to be. Whereas we have looked upon the changes that have occurred about teeth, as being directly both the result and the measure, in general, of the infection process, we found, contrary to the accepted interpretations and expectations, that the structural changes do not denote either the quantity or quality of the infection in a sense that we have understood.

In Chapter 1, we found that there are very definite limitations to the capabilities of the Roentgen-rays in the matter of disclosing either the presence or extent of dental infections.

In Chapter 2, we found that the organisms involved in various dental infections may have any of the several biological characteristics of the various groups of streptococci, irrespective of either the type of local expression in the affected tooth or the systemic involvements of the patient.

In Chapter 4, we found by an analysis of many hundreds of individuals that they do not have comparable histories and also that they do not have comparable expressions of similar dental infections; that they do tend, however, to divide into groups, the members of which groups are so similar as to be directly comparable.

In Chapter 3, we found that a given dental infection may express itself in a large variety of local ways in the local tissues about the tooth, and that all these variations depend upon conditions which are inherent to the patient.

In Chapter 5, we found that there is a very direct relationship between the type of the local expression of the dental infection and the systemic reactions.

In Chapter 6, we found that absorption might be caused by other irritants than dental infections.

In Chapters 7 and 8, we found that in both dental caries

and periodontoclasia there is a very definite tendency of pulps to become infected and undergo degeneration changes with the approach of infection from these sources.

In Chapter 9, we found that people with a tendency to rheumatic group susceptibility have also a marked susceptibility to dental caries.

In Chapter 10, we found that the gingival infections do not tend readily to develop about the teeth of people with marked susceptibility to rheumatic group lesions, and their active process is more frequently found in individuals at a time when they have not a susceptibility to rheumatic group lesions.

In Chapter 11, we found a marked relationship between the tendency to gingival infections and a tendency to extensive periapical absorption with a given dental infection.

In Chapter 12, we found that the extent of the absorption not only is not a measure of the danger but frequently is an accompaniment of complete absence of rheumatic group lesions.

These data have revealed a progressive type of rarefaction with an increase of systemic defense, in contradiction to the accepted theorum that the extent of infection is a quantitative measure of the infection and hence of the danger (or the extent of systemic involvement). This seems like a paradox, and it is not strange that frequently when we have expressed this new interpretation, that the first reaction has been not to accept it. Incidentally, this was our own reaction for a long time.

Let us study the nature of the forces operating about the root end of an infected tooth whose pulp is already putrescent. This degenerating pulp consists of the products of bacterial activity including the bacterial toxins, tissue degeneration products, living and dead organisms, and mechanical interferences such as pressure of fluids and presence of gases. A first result of all irritation is stimulation. The extent and nature of this irritation determines the extent and nature of the inflammatory reaction. There will be an engorgement of defensive factors in the surrounding tissues, the marshalling of which requires marked dilatation of the blood vessels to take care of the additional blood for the defensive and offensive operations. This constitutes the first stage of inflammation. With the marshalling of lymphocytes, bacteriolysins, antitoxins to neutralized toxins, etc., there will be a marked liberation of antagonizing substances and their products into the field of no man's land at the point of most intense battle between the invading organisms and the defending tissues, which is di-

rectly the result of the warfare, for Nature is trying to establish a quarantine. If she succeed, it will only be because she maintains that active warfare. But such a warfare means a constant accumulation of the products of the warfare, phagocyted leucocytes, neutralized toxins, all taken care of by Nature's mechanism or irrigation to eliminate pollution. Which will require the larger refuse disposal irrigation system, a very mild local reaction or a very severe one? There is no question as to which will. Our roentgenogram records some characteristics of the battlefield, whether it be large or small, or whether a truce be on, or whether, as it may be, no adequate quarantine has been established.

A study of individual cell reactions shows that the difference between an active reaction in one direction or its complete reversal is dependent upon the amount of stimulation of the cell. For example, the same cells that lay down some calcifying structures will proceed immediately to take them up again if pressure is applied to them, and this reversal process may go on as long as those tissues live. Similarly, tissues may be made to lay down bone or take it up again with other forms of irritant, as, for example, retention of heat, prevention of radiation, chemical vapors, contra-irritants, etc., etc.

But we have said that, in general, the organisms are not different in different cases, or at least that the effects produced are not the result of difference in definite strains of organisms. What, then, is the force that determines whether or not this given irritant, the bacterium involved, (which as we have implied or said we believe to be quite similar in the various cases except that it is made different by its environment) will produce a large or small chamber in the bone about the root apex? We have only to think of the wide range of effects that will be produced on various individuals by the same irritants. For example, mosquito bites have almost no effect on some people, while on others they not only produce violent local inflammations with swelling and great pain but such violent toxic effects on the whole system as to make the individual positively ill. The difference is not in the irritant in this case; it is in the reaction to the irritant, which factor is primarily, an activity of the host called forth in response to the invading irritant. Until we have had typhoid, we have little or no attacking power against the organism of typhoid when it gets into our blood stream. When we have had that in-

fection in our system for a sufficient number of days, we have built up a mechanism of attack; and the difference between an individual with that defensive mechanism which constitutes his immunity more or less perfect ever thereafter, and the individual who has no immunity and becomes readily a culture ground for the organism, is precisely that power to react.

Let us think now of the phenomena of local reaction to dental infection in terms of reaction rather than in terms of attacking power of the invading bacterium, and apply this interpretation to the various experimental problems as we have been reviewing them. Returning again to the problem of Chapter 4, Systemic Structural Changes, we found that human beings divide themselves into groups, the members of which groups are comparable to each other, while the members of the different groups are not comparable; and the fundamental differences between these individuals on this basis are those qualities which make them competent to react against rheumatic group infections. Those with an absent susceptibility have so good a defense that they do not develop rheumatic group lesions. Their local dental infections are invariably accompanied by extensive areas of rarefaction; in other words, an efficient and adequate local reaction. The second group, those with an acquired susceptibility, have had that high defense, until by overload it has been temporarily broken. In this state of acquired susceptibility their local reactions about their dental infections are very poor. In the third group, those with an inherited susceptibility, we find that in the progressive groups, from mild inheritance to very strong, there is a progressive lack of ability for defense against the invading organisms with a consequent progressive development of lesions as the local reactions become less and less acute. In other words, as the defensive reaction diminishes at the point of invasion—namely, the infected tooth—the systemic susceptibility increases, whether acquired or inherited, except that the prognosis is very different in the individual whose defense is normally high from that of the individual in whom it is normally (by inheritance) very low; and similarly, we might apply this new viewpoint to all the different phases of the problem as expressed in this series of researches.

Let us apply this interpretation to the gingival infections. Figure 262 shows a typical and extreme case. Seldom do any of us ever see a mouth with so much free pus exuding from around the teeth. The bicuspids and incisors are so literally floating in pus that with every movement it exudes in all directions. Note the

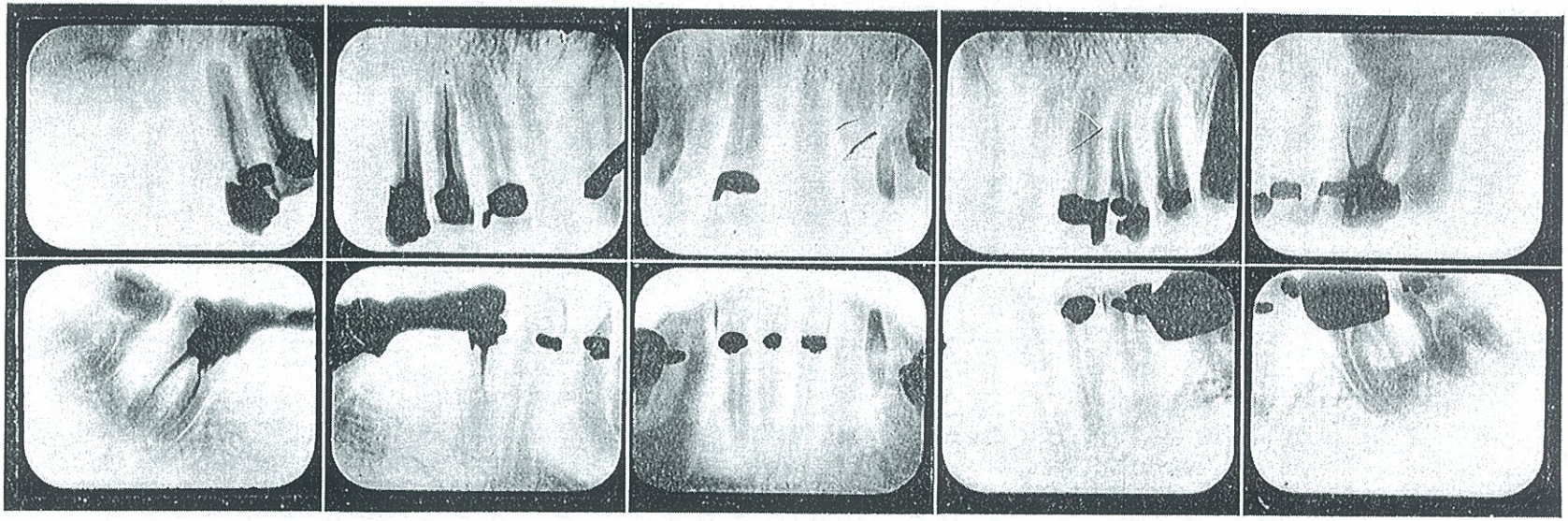


FIGURE 262. CASE NO. 1268. ROENTGENOGRAPHIC APPEARANCE OF A CASE WITH A PROFUSE FLOW OF PUS, EXUDING WITH EVERY MOVEMENT OF THE TEETH. NEITHER THE PATIENT NOR ANY MEMBER OF THE FAMILY GROUP HAD HAD RHEUMATIC GROUP LESIONS. CHEMICAL ANALYSIS OF BLOOD AND URINE REVEALS THAT HE HAS ALREADY A SEVERE HYPERGLYCEMIA AND GLYCOSURIA. THE PATIENT HAD NO SUSPICION THAT HE HAD DIABETES.

very extensive alveolar absorptions. Surely, if any person would be sick, if a quantity of pus could make him so, this man would be. But what are the facts? He is forty-six years of age, has never had a moment's rheumatism or neuritis, or any other affection of which he knows; nor have any of the members of his family, either on the father's side or the mother's side, or brothers and sisters. His mouth has had wretched care; deposits are everywhere; there has been no worthy effort at prophylaxis. Why has he not broken? Because he has established an adequate quarantine, though at a terrific cost, for the battle-ground has extended until it has involved tissues nearly to the apices of many of the teeth and quite to that point on several. What is his classification? Up to the present—absent susceptibility. How long will it be so? Impossible to tell but probably not long, for already his urine shows 4.46 per cent of sugar, and his blood 295 mgs. of sugar per 100 cc. (Normal threshold of danger about 120. Normal blood sugar 70 to 100.) The ionic calcium of his blood is 12.32 mgs. per 100 cc., one and one-half above normal. His mother had diabetes. How long will the quarantine be kept up? Until his defense goes down with Flu, dental infections, overwork, great grief, or any of the many complications and contributing factors. Then what will happen? When the quarantine is withdrawn from all this area of attacking enemy, it will rush in and overwhelm his system; and this type of man often goes down like an avalanche with diabetes, nervous breakdown, Bright's disease, etc. This man's impending danger is already upon him as an unsuspected diabetes, though he thinks he is well, for the islets of Langerhans of his pancreas are probably already diseased either from the dental infection or other sources. He may be helped by the administration of their extract, insulin, or the pancreas injury or disfunction may be related to other causative factors than the dental infection. These are discussed in the chapter on Diabetes. What will the prognosis be? If the source of infection is removed and his defenses thereby restored, he will tend readily to come back to his normal, which is high, provided that the functioning of some fundamental tissue or organ has not been permanently impaired. But just here is his great danger. What will be the expression of his periodontoclasia when he has lost his defense? Much less pus formation because there is much less local warfare. Indeed, it will become the camping ground of a new type of organisms. Streptococci and staphylococci, chiefly

the former, will take up their abode in the necrotic hard and soft tissues. Fusiform and spirochetes will largely disappear with the reduction of the alkalinity of the exudate poured into the gingival pockets and the cutting off of special nutrient materials on which they depend. Where will the new invaders, the streptococci and staphylococci, go while that defense is broken? They will have a pass practically to every part of the body, for that is what constitutes the absence of reaction.

There are many phases of this problem upon which important researches must be conducted. In the chapter on Ionic Calcium of the Blood in Relation to Focal Infections and Systemic Defense, and as demonstrated in the many clinical histories in the succeeding chapters in Part Two, we see that there is an optimum ionic calcium of the blood below which there is a tendency to the rheumatic group lesions, and above which there is a tendency to periodontoclasia, diabetes, acidosis, osteomalacia, etc. The former tends to be associated with condensing processes in association with rarefactions. Carbohydrate metabolism, alkalosis, alkalipenia, acidosis are all related factors and they thereby become direct means for checking the defensive factors and pathological tendencies of the individual.*

In our introduction we referred to the fact that internists and dental practitioners have been saying, "How can it be true that dental infections are such important etiological factors in rheumatic group affections when so many individuals have such large quantities of infection present in their mouths, and yet have none of these disturbances?" This new interpretation seems to explain for the first time this paradox, for the thing they were seeing was the surest kind of proof of this type of reaction of which we are speaking; and the cases in which the reaction was absent were interpreted not to have any occasion for reaction, as will be abundantly demonstrated in our clinical cases. The individuals with the acute rheumatic group lesions are, in the great majority of cases, those with no more cause than this group we have just been discussing, but they are individuals who are not maintaining the adequate local quarantine about their teeth.

But, as we have seen, we are not dependent upon the indirect evidence to establish that this is fundamentally a warfare between an invading organism with its mechanisms of attack and defense on one side, and the host with its defensive mechanisms and de-

*Notwithstanding the above general principal, some types of arthritis are locally characterized by degenerative processes and systemically accompany abnormally high ionic calcium of the blood.

vices of attack on the other, which latter are established and maintained by the host as a permanent system of quarantine so long as the dental infection exists. In addition to the indirect or clinical data, to which we have referred, we have seen in Chapter 38, The Nature and Function of the Dental Granuloma, and Chapter 41, Variations in the Defensive Factors of the Blood, that both the granulomatous tissue, when in good functioning condition, and the normal blood structures, particularly the leucocytes, furnish substances which not only have the capacity for inhibiting the growth of the organisms, but actually devitalize and literally digest them. It is not an accident or a mere coincidence, but a fundamentally associated fact, that the individuals with that type of blood and with that type of granuloma are those without clinical histories of rheumatic group involvements, and this notwithstanding the abundant evidence in their cases of an ample infection in the involved teeth. Our problem, then, simplifies itself to a study of the relative and actual efficiency of the local and systemic mechanisms in conjunction with the presence and absence of dental infection; and a very small quantity of infection, existing without the presence of the defense, may do the individual much greater harm than will a very much more extensive infection in the presence of these mechanisms of defense.

SUMMARY.

We would briefly express our interpretation of the Phenomena of Local Reaction as follows:

The structural changes which develop about infected teeth are expressions, primarily, of the type of reaction of the host to this irritant and, as such, are therefore, when understood, a direct means for interpreting that individual's defensive mechanism.

CHAPTER XLVII.

INTERPRETATIONS.

THE PHENOMENA OF SYSTEMIC EXPRESSIONS OF DENTAL INFECTIONS.

DISCUSSION.

The researches which we have reviewed in the preceding chapters have many of them been carried out to ascertain further fundamental data regarding the relationships between systemic expressions and focal infections, with particular reference to dental focal infections. In Chapter 4, which is a review of a study of the factors which individuals have in common with regard to susceptibility to, or immunity from, systemic involvements of the rheumatic group type, these indicated that this quality is persistently present in certain individuals and persistently absent n others, while in still others it is a variable quality appearing only under severe stress and overload, and that these qualities of susceptibility and immunity are not related to the particular type or strain of organism present (Chapter 2) or to the particular type of lesion. It is also demonstrated that this quality is very closely associated with the forces which control in the processes of heredity. For example, there were more cases of heart involvement in one hundred of seven hundred families than in the other six hundred.

In Chapter 5, in studying the relationships between local and systemic infection, we recorded the following conclusion: That a given infection may express itself by causing an absorption, even extensive absorption, or may produce very little absorption. or none at all, of bone tissue, and may even produce condensation of the bone, *all depending upon inherent conditions of the patient or host.*

In Chapter 9, we found that there was a marked relationship between the predominance of caries and the susceptibility to systemic disturbance.

In Chapter 10, we found that susceptibility to systemic involvement was not in proportion to susceptibility to periodontoclasial infection.

In Chapter 11, we found that there was a direct relationship between the tendency to gingival rarefaction and bone absorption and extensive periapical rarefaction and absorption accompanying periapical infection.

In Chapter 12, we found that the relation of the extent of the absorption to the danger was, in general, in inverse proportion to the latter for a given infection.

In Chapter 13, we found that the discharge from a fistula from a chronic periapical abscess, is made up almost entirely of neutralized products, leucocytes and phagocyted organisms.

In Chapter 16, we found that comfort and serviceableness were not necessarily dependable criteria or evidence to be depended upon as symptoms.

In Chapter 21, we found that, whereas the normal body has what may be normal as a defense for that patient, that standard may be greatly lowered by various types of overload, such as acute infections, grief, pain, hunger, focal infections, etc.

In Chapter 22, we found that the quality of elective localization on the part of bacteria is a relatively transient quality which since it is easily lost by placing in a changed environment such as an artificial culture medium, rapidly disappears and, in general, seems to be directly related to the environment furnished by the circulating forces of the patient's body rather than the local dental conditions.

In Chapter 24, we found that this quality of tissue affinity or elective localization is one which relates largely to the particular organ or tissue rather than to the entire system, with, however, systemic factors, one of which is calcium metabolism.

The similarity of these studies reveals that the quality of susceptibility or immunity to systemic involvements is not determined by qualities and conditions which obtain in the focus of infection, but have to do with various tissue defensive factors together with the general defensive factors of the body; and that while the local conditions are not the primary factor in the systemic susceptibility, there are distinct characteristics of the local expressions of the focal infection in both the condition of marked systemic susceptibility and the condition of marked systemic immunity; and, further, that these systemic qualities, which constitute that susceptibility, have to do with the ancestry and progeny; also that these qualities relate to individual organs and tissues of the body in such an orderly manner that we can see

distinct evidence of true mendelian factors. In addition to these inherited susceptibilities, tissues are greatly influenced by overload changes, among which are those which disturb nutrition and metabolism. These may be divided into groups: Infections such as influenza which suddenly and very definitely destroy the normal defense to streptococcal infections, so much so that one of our high authorities has suggested that when the people living in our civilized communities of today die, in the great majority, the final blow will be struck by an organism they are carrying within their bodies, and for which they have, under ordinary conditions an ample defense. I found, as I have shown in Chapter 21, in my analysis of conditions in hospitals in the Flu epidemics that the incidence of systemic complications with, and following the Flu, was about two and one-half times greater among patients with extensive dental infections than in those without dental infections. Next to influenza we would be inclined to put pregnancy as a condition of overload which predisposes to rheumatic group disturbances. Fear, grief, worry, focal infection, etc., are all very direct influences in reducing normal defense.

A very important contributing factor to a condition of susceptibility is found in disturbed nutrition; by which we do not mean people who are not in position, by sheer poverty and uncontrollable circumstances, to get food, but we will include vast numbers who are starving their normal defenses by improper eating. Another and very important factor has to do with the nature of the focus of infection; whether its contents are under pressure, whether the quantity tends to overwhelm the available defensive factors, or whether they had tended by long duration to exhaust the defensive effort. It is said of the Eskimos on certain northern islands, that every Eskimo who was exposed to measles died; yet, for centuries, no Eskimos died from measles because no Eskimos were exposed to measles on said islands.

It seems in large measure true, exceptions to which I will discuss elsewhere, that individuals with marked susceptibility to rheumatic group lesions may for long periods, as are the Eskimos, not be affected because of complete absence of exposure to streptococcal proliferation within their systems; and, herein, lies our great danger. A dental infection is safely and permanently protected even within Nature's fortress. Indeed, it develops and supplies the organisms from within an armored blockhouse into which none of the defensive factors of the host can successfully enter to

exterminate them, yet into which that host furnishes a continual supply of pabulum and food in the circulating plasmas brought to that tooth. Under what conditions will the defense be high enough? Just so long as every organ and tissue of that body can safely defend itself against the circulating poisons sent out into the system from that fortress for creating diabolical poisons, provided that the larger proportion of the toxic products and invading organisms may be destroyed as they leave that fortress.

We find ourselves, then, face to face with the same problem which we had in the preceding chapter, the problem of effective local reaction about the tooth. If the local reaction is adequate, it will, incidentally, as we saw in the last chapter, produce extensive rarefaction as part of the process of warfare. It will primarily preserve the rest of the body from exposure by the maintenance of that efficient local quarantine. When that quarantine breaks down, that tissue which is most susceptible because of inheritance, with or without an additional overload, will be the one that will break. If all tissues have normally a very high defense, the break will, in all probability, come in the nervous system. When will it come? That depends. When the overloads and normal body defenses together have reduced the balance, so the pendulum swings in favor of the attacking organisms. It may not be until ninety years of age; it may be at sixty; or it may be at thirty; but it *will* be, sometime, for it is a fight to a finish with every one of us and, ultimately, we lose. But both our clinical data and our experimental research demonstrate that, only that individual will reach the eighty or the ninety mark and carry his dental infections, who also carries until that time a well vascularized special tissue which Nature will build about the source of exit of his dental infection into his system. Whether we call it a granuloma or otherwise, when it becomes a degenerating, inefficient, defensive membrane, the warfare is not completed at the first line trench, and some organ or tissue will break.

CHAPTER XLVIII.

INTERPRETATIONS.

THE PHENOMENA OF RELATIONSHIPS BETWEEN LOCAL AND SYSTEMIC EXPRESSIONS.

DISCUSSION.

In the three preceding chapters we have discussed and suggested interpretations for the various data presented by the researches on dental infections from the standpoint of the phenomena of bacterial invasion, local reaction, and the phenomena of systemic expression, and found that underlying each were certain consistent and quite regularly observed expressions which are sufficiently constant to be looked upon as being the result of definite laws of cause and effect. In this chapter we desire to study the two latter groups of phenomena with a view to observing whether in some particulars they may be related each to the other, or both to the same cause. In general, these researches have disclosed that the quality, which we recognize as an ample systemic defense, is found in an individual who, when he or she has a dental infection at a root apex, tends to have an extensive reaction with an accompanying rarefying osteitis. We will, in this chapter, use this term as indicating that local condition, whether at a root apex or accompanying an irritation at a gingival margin, for these studies have shown that these individuals with high defense show this same marked tendency to absorption of bone as a result of irritation, regardless of its location, and that these individuals readily develop the clinical condition which we have come to look upon as periodontoclasia, or pyorrhea alveolaris; and, conversely, we have seen that individuals with a low systemic defense to streptococcal infection, tending to express itself systemically as some of the rheumatic group lesions, have local dental infections which tend to express themselves as an absence of extensive rarefying osteitis, or with a definite condensing osteitis, and in whom gingival alveolar absorption is almost completely wanting; in other words, very little periodontoclasia, or pyorrhea alveolaris.

Are not these two conditions of local type of expression and systemic susceptibility or immunity, symptoms of a common

condition or effects of a common cause? To approach this complex question let us look at some of the serological data to see if with even our present meager knowledge of blood, saliva, and urine chemistry, there are any items that will throw light upon this problem. If we will take a patient whose general history has shown that his general condition has been one of an absence of involvement, but who has, because of acquired conditions, developed that state which we speak of as susceptibility to some type of rheumatic group lesion, we should, by a careful analysis of the various sera of the body, get information that would at least be suggestive, though it will only be by a large number of studies that we will be justified in making conclusions.

The variations from normal in various factors which may be found within the body during life, may have a wide or narrow limit of change, dependent upon the nature of that factor, both in health and disease. For example, there may be a relatively wide range of variation in body weight in food ingested, liquid ingested, excreted, and radiated, or even carbohydrate tolerance, the threshold of which may be passed for considerable periods; in contrast with which, other factors have very slight deviation from normal, (or rather, that the range of variation, both in health and disease, will be very narrow.) This will be illustrated by the constancy of the hydrogen ion concentration of the blood, which variation in normal is not measurable by the usual means, and in disease can vary but a very small measurable amount without causing death; whereas, in these same individuals, the hydrogen ion concentration of the urine may vary from pH of 2 to pH 8, and of the saliva, from pH 3 to pH 7.8.

Another factor that is relatively constant is the calcium present in the blood, which may vary from 9 to 11 mgs. per 100 cc., and is seldom below 9.5 in normal. The calcium present in the urine seldom exceeds 11 mgs. per hundred cc., and in the saliva has a relatively wide range in calcium oxalates and in calcium as oxides. In this supposed patient we have a distinct tendency to rarefying osteitis and calcium absorption, expressed both in radiolucency of bones and reaction to inflammation, both in the mouth expressing itself as periodontoclasia, and in the involved joints as a type of rheumatism. This suggestion of a disturbance of the calcium balance, or of the calcium controlling mechanism, is emphasized by the depressed calcium content of the blood and the increased calcium content of the urine and saliva. While it

is impossible, in the present state of our knowledge of calcium metabolism, to affirm which factors are causative to others and which are symptoms as the result of some as yet unknown cause, it is strongly suggested that the calcium disturbance of this case is in part the result of the bacterial invasion of the gingival tissues, and the absorption of toxic substances which are the products of bacterial reaction in tooth structure. For example, we have many illustrations of disturbance of the thyroid from dental infections and other causes. A disturbance of thyroid function may in those cases, be the controlling factor in metabolism, which determines the amount of depression of the calcium balance in the blood, the rate of calcium assimilation of food, state of calcium hunger of the system, expressing itself in part by the taking up of calcium readily from inflamed osseous tissues, and its wastage as overflow in the excretion products; or, as is more probable, both the thyroid and parathyroids may be so involved and so contributing.

We do not present this as a conclusion, but as one of the suggested interpretations of the group of phenomena presented in this case; and this case represents a group, and it will be by enlarging our information of the various individuals in such groups, that we will be most likely to advance our knowledge of this phase of the problem. (One of the hopeful ways of enlarging our knowledge of this and similar types of pathology will be by studying similarly as large a number as possible of individuals grouping naturally into this and other groups.)

When we review the data developed in the preceding chapter, several factors have been greatly emphasized. Rabbits will continue for weeks and months to show a constant calcium without a variation of more than a fraction of a milligram. If within twenty-four hours after a piece of the infected root has been removed from the human, it is placed beneath the rabbit's skin, the ionic calcium of its blood begins to change and the change is progressive and continues unless that animal be capable of maintaining an adequate defense immediately about the tooth. In all cases where the animals have built up such a defense, the local expression has been one of concentration about the implanted piece of a highly vascularized connective tissue; and when this tissue is finally broken down, in those cases in which it is, the systemic defense soon gave way; and, similarly, as the rabbit's condition took on certain characteristics, such as depressed ionic

calcium with loss of weight and progressive change toward death, very frequently the patient, from whom that same tooth was extracted, progressively gained in weight, had a progressive change in the ionic calcium of the blood, and lassitude gave way to a condition of well being, etc.; and, similarly, a patient suffering from leucopenia progressively developed an improvement in that factor of the blood, and the rabbits beneath whose skins the tooth or a piece of it was planted, proceeded to develop a leucopenia in many cases. It is, therefore, not an accident that the rabbits, who resisted the infection, practically always built a defensive tissue about the implanted infected tooth.

There is really no way that this relationship between the local and the systemic expressions can be so clearly seen as by watching a dental clinic which furnishes a wide assortment of conditions; for, while it is true that few cases can be said to belong to any one grouping with complete freedom from aspects of some other basis of grouping, the general expressions will be so constant as to emphasize the constancy of these relationships.

CHAPTER XLIX.

INTERPRETATIONS.

INHERITED SUSCEPTIBILITY AND MENDEL'S LAW.

DISCUSSION.

In the four chapters preceding, we have reviewed the phenomena of infection and local and systemic reactions and their relationships to each other. In these we have summarized the researches of previous chapters. In many of these studies and analyses we have found that while individuals are not comparable as a whole, they tend to divide into groups, the members of which are directly comparable. This general tendency to grouping is related directly to the presence or absence of a susceptibility to rheumatic group lesions. In the main, they divide into two groups: Those who are and those who are not susceptible; except that of those who are not susceptible, they may become so, usually temporarily, by overload; and when they do break, the tendency is to break in the overloaded tissues and organs, or the nervous system. The other group with natural tendency to susceptibility we have found to have that quality in common with other members of the same ancestry and with one or both sides of the ancestry, though this quality may be present in a strong or weak degree of dominance. In this chapter we desire to study these individuals and the data of these researches with particular reference to the fundamental laws of heredity, usually spoken of as mendelism or mendelian traits.

Mendel was an Austrian monk, the centenary of whose birth has recently been celebrated, but whose work made no impression upon the generation to which it was given nor for some succeeding generations, and it was not until the great principle was rediscovered that any importance was given to his writing. He found in growing his garden peas that the interbreeding of different types developed new types which had definite relations to the old, and that these followed a law of proportion. This has become so fundamental a part of all the modern thought and teaching of biology that it is generally accepted and taught as being just as constant a law of cause and effect as the laws of magnetism, gravita-

tion, and light. In general, the fundamental tenets of mendelism may be expressed about as follows:

(1) Characters are inherited as units. That is, that my boy has a nose like mine, independent of whether other characters such as hair, eyes, stature, etc., etc., are alike.

(2) Characters are not inherited, but determiners for them are. That is, that my boy does not inherit my nose in any sense but that he inherits determiners which provide for a nose like mine.

(3) My boy does not inherit anything from me that I did not inherit from my ancestry. In other words, that he and I are half-brothers by different mothers, and each one of us has the same, or in part the same, type of determiners that have been handed down through the long chain of ancestry.

These fundamental principles are modified more or less widely for different types of unit characters. For example, some characters are inherited only through the mother's side of the ancestry, as, for example, the quality of color blindness. Others are inherited in equal dominance from both sides of the ancestry. Still others denote the presence of a dominating determiner, such as brown eyes; whereas blue eyes denote simply the absence of a determiner for brown pigment. In still others, one character tends to dominate, while others are in mathematical proportion. To illustrate:

Crossing blue Alsatian fowls with white, will produce an equal number of blues and whites—namely, one-fourth of the total of each of these two colors—whereas one-half of the total will be neither blue nor white but will be speckled; and these speckled fowls will produce the same ratios of blues and whites, when crossed, as will the whites and blues from this same ancestry. Whereas, if white guinea-pigs are crossed with black guinea-pigs, the first generation will be all black guinea-pigs, which black guinea-pigs, when crossed, will contain determiners for both whites and blacks; and in the next generation, there will be three blacks to one white, the black dominating in about this proportion over the white. Important experiments have been made to ascertain the seat or origin of this force in heredity, one of which was to remove the ovaries of a white guinea-pig and in their place put the ovaries of a black guinea-pig. She was then crossed with a white guinea-pig, and, whereas the offspring of all matings of two white guinea-pigs could only produce white guinea-pigs, in this case, the crossing of these two white guinea-pigs, the female of

which carried the ovaries of a black guinea-pig, produced only black guinea-pigs. In the next generation these black guinea-pigs carrying the determiners in the proportion of one to three of whites to blacks, would produce one-fourth white guinea-pigs and three-fourths black guinea-pigs. It is, accordingly, established that the determiners are resided in the cells of the sex organs and are transferred from the sex organs of one generation to those of the next generation independently of all other cells of the body.

In the light of these data regarding the laws of heredity, let us review our findings regarding susceptibility and its expressions.

In Charts 43 and 48 we found that there was a very marked tendency for individuals with rheumatic group lesions to produce offspring who tended to be susceptible to rheumatic group lesions. This is so marked, that it becomes directly a means of classification where the histories can be obtained with sufficient completeness. But this is not new. Sociologists have long been furnishing data demonstrating that heart disease, for example, tends to run in the family, and similarly, many other affections; and while our later developments have demonstrated that rheumatic group lesions are quite largely the result of infective processes, this does not change, though it puts new light on the already well established principles as laid down by statisticians. But there is an important new development which has come out of these researches, which, so far as I know, has not been developed previously; namely, that the tendency to rheumatic group lesions of a given type, for example, heart or rheumatism, etc., follows a law that corresponds to this general law of mendelism: namely, *that inheritance susceptibility of various organs and tissues is a unit character so far as different organs and tissues are concerned, as completely as with color of skin, hair, and eyes, length of nose, height of stature,* etc., etc. In other words, we have shown in Chapter 4 that a careful analysis of the lesions of various organs and tissues demonstrates that where they do appear, they appear in large numbers of a family. For example, as shown in seven hundred families, there are more cases of heart affection in one hundred families than in the other six hundred.

CHAPTER L.

INTERPRETATIONS.

AN INTERPRETATION OF RADIATION REACTIONS.

DISCUSSION.

Previously, in Chapter 27, we have discussed researches on the effects of different types of radiation upon normal and pathological tissues. From these it has been shown that when teeth, from the infection of which there is an extensive flow of pus, are exposed to the Roentgen-rays of suitable length, one of the very conspicuous effects is the diminution of the quantity of pus produced, so much so that it is a very frequent experience to see fistulæ of long standing, from apical root infection, close quite rapidly after the raying in even such amounts as would be used in making a few roentgenograms, and particularly so with the former types of tube in which the penetration was very low, much of which radiation was absorbed by the tissue. Our researches disclosed that extensive periodontoclasial lesions, if judged solely by the criteria of pus, were apparently greatly benefited by raying with this type of radiation. Quite different effects are produced on pathological tissue of the mouth, as, for example, periodontoclasia, or pyorrhea alveolaris, with different types of radiation.

We are all familiar with the tanning effect of the sun's rays upon the skin and with the life-giving effect to all vegetable and animal life, which comes from these rays. We have referred in Chapter 27 to the increase of rickets in dark and cloudy countries and areas, and its cure by the subjection to either the sun's rays or to mercury vapor arc radiations.

Early in the history of radiation studies, Finsen discovered that by using large lenses and concentrating the sun's rays and taking the heat out of these by passing them through suitable substances, such as water, these radiations had marked effect on certain chronic ulcerative diseases, such as lupus vulgaris, and also on deeper diseased conditions. Following out and developing this line of work, various types of arc light lamps, including mercury vapor arc, have been and are used to generate rays having lengths approximating those that have been found in the sun to be of marked curative value.

Similarly, radium had been found to possess qualities which are very unique and not entirely unlike those of the Roentgen-rays. For example, probably today more epitheliomas are treated with radium than by any other means, if not by all other means combined; and in the early stages this treatment is almost specific in terminating the tendency to malignant cell proliferation. The only reason that it is used most for cancers of external surfaces is because of the penetration, only a small proportion of the rays passing though to deep layers.

Periodontoclasia, or so-called pyorrhea alveolaris, is a very general term and is applied to a great variety of lesions which are, in the main, different stages of a general process, and the same periodontoclasia pocket in those different stages will furnish as wide a range of type of tissue, as will be found in a rodent ulcer at one extreme and a bee sting in the other; and yet in all its various extreme and intermediate stages, it is thought of, and spoken of, as the same lesion. In its early stages tissues, with great capacity for reaction to irritation, are making a normal and violent effort to resist the attacking irritant, with the consequential effect of all acute inflammations: namely, absorption of tissue, flooding of the area with lymph and leucocytes, which, together, make what is readily considered an abundant flow of pus. Flooding this tissue with rays of the variety of the Roentgen-rays, destroys the capacity of those cells to make that normal and efficient reaction, and the reduction of the pus in the presence of the maintained irritant is not an evidence of the removal of the irritant by the creation of a toleration and lack of reaction to it. True, these tissues may be those of a patient having exalted capacity for reaction, which I wi l discuss later.

A later stage of this same periodontoclasia pocket is one in which no pus is generated. Incidentally, the bacterial flora in these different stages quite considerably change; but in this final condition of exhausted function of reaction, we have the type of periodontoclasia pocket which does not respond to treatment. In its early stages with its acute reactivity, repair is most gratifying and rapid with removal of the irritant. In this latter condition the patient's health is endangered to a much greater degree, for in the former condition Nature is maintaining a pretty successful quarantine; in the latter, she is not doing this because tissue of low vitality often is related to definitely dead alveolar tissue, (which dead bone is abundantly infected with

streptococci which readily enter the system,) and from the old chronic periodontoclasia pocket we may have serious and extensive, though usually not sudden in development, systemic involvements. When tissue in this state is treated with Roentgen-rays and radium, and already depressed cell function is still further depressed, and if results are to be judged by the one standard of flow of pus, even this type of condition may seem to be improved, or at least not to be made worse, while in reality, it has really been made worse. Our researches have showed that when this type of tissue is exposed to radiations of suitable length, there is a very definite tendency to increase the cell activity or reaction capacity of the tissue, with the effect that again there is thrown out the exudate, and again a capacity for repair accompanied by a change of bacterial flora from the chronic stasis of the poorly reacting tissue to that characteristic, or more nearly so, of the active periodontoclasia pocket in its early stages. This, then, becomes immediately a means for observing both the type of pathology involved, and the effect of medication, particularly by means of radiation. My interpretation of these phenomena is that we are dealing with the same problem that we have discussed in the three preceding chapters—namely, types of reaction—and when we can know more about the mechanism within the cells themselves, we can understand more exactly by what means radiation produces its effects.

When the larvæ of flour mites are exposed to radium radiation of the proper amount, the effect is completely to change the life cycle, and the small moth will continue to live in its caterpillar stage, while those of its fellows, which were not exposed to the rays, have passed through three complete cycles of caterpillar to moth. Similarly, when certain plants are exposed to the radiations of radium, while they continue to live, they do so as stunted specimens. Something has happened which radically changes the vital forces within the cell.

Whether these changes which we are considering as result of radiation can be harnessed and made to modify quite largely local tissue reactions, only further experimentation can establish. The evidence to date, however, strongly suggests that great progress will be made along these lines. There are, however, as evidenced in the large number of histories which make up a part of these studies, abundant illustrations that back of the local expression is a very definite systemic capacity, which relates not only to this

individual, but to many or most of those having the same ancestry. We are dealing, then, with forces which are variable and which, while subject to influence by forces which sift and mold Nature's fundamental potentials, tend largely to follow the order of their kind.

CHAPTER LI.

INTERPRETATIONS.

THE PHENOMENA OF SENSITIZATION REACTIONS.

DISCUSSION.

In Chapter 30, we have discussed the quality or symptom of anaphylaxis or tissue sensitization. We called attention to the common illustrations of this condition known as hay fever, asthma, and certain skin disturbances. We also demonstrated that similar conditions may be and frequently are produced by dental infections. By reproducing these symptoms in animals, we demonstrated that we were not dealing necessarily with bacterial invasion. For example, the filtered washings of the crushed teeth of a patient, suffering from a violent inflammatory process of the nose and air passages with acute inflammation of the eyes, accompanied by bloodshot and extreme lacrimation, were injected into rabbits and produced in forty minutes a similar bloodshot condition of both eyes and acute rhinitis. This reaction occurring in forty minutes is, of course, not an anaphylaxis.

While the studies of sensitization reactions have not advanced so as to furnish a definite conception of the mechanisms involved in this reaction, they have been carried far enough so that the interpretation of many of the phases are quite generally accepted. Some of these are that there is a reaction between antigen and antibody; that this antibody does not exist natively in most animals, but that it is created by the first injection or entrance of the antigen in question into that animal's system, and that this process of reaction which creates the antibody, which latter unites so violently under certain conditions, if the same antigen is introduced, is closely related to the process known as immunity. To illustrate:

If most any protein as, for example, egg albumin, blood serum, tissue extract, or milk, is injected into the circulation in even a small quantity, or even in a relatively large quantity, it will produce no effect. If, however, a small quantity of this same protein is injected into the blood stream or tissues of this animal, after a period of six to twenty-eight days, a violent reaction occurs which

in many animals terminates in a few minutes in death with spasmodic contractions of the bronchioles, but with a definite chain of symptoms beginning with excitability, then irritations of the nose and skin, then labored breathing, and finally with a dyspnea produced by the maintained contraction of the bronchioles, the heart going on beating for some minutes after breathing is stopped. This reaction may be produced by the introduction into the system, as a first or sensitizing dose, of a quantity of material incredibly small. One millionth part of a gram, as a first or sensitizing injection, will suffice to induce that animal to develop the antibodies, which latter will react very violently with this same protein antigen, if introduced after the incubation period. This condition of maintained ability to react, compares in many ways with the ability to react to a second invasion or exposure to a contagious disease, to which the individual has by the first exposure to an infection built up a capacity for reaction, which we speak of as immunity.

Similarly, individuals become sensitized to proteins which enter the body not only through the air passages, as in hay fever, but from ingested foods. Not infrequently, in fact very frequently, individuals are sensitized to egg, milk, banana, certain cereals, in fact almost any food product; and in this case, it is believed that the alimentary tract allows some of this unsplit protein to enter the system in sufficient quantity, to be acted upon by the antibody that has been developed by the previous entrance into the sytem of that protein, and all that is needed to cure this sensitization to a given food product, is to eliminate that food product from the diet, just as individuals subject to hay fever have only to protect themselves from the particular pollen to which they are sensitive by going to a community where that species of plant does not grow. Accordingly, individuals living on limestone belts find relief in going to areas with laurentian formation where the flora will be entirely different.

In the case discussed in Chapter 30 in which the patient suffered from a violent rhinitis and coryza, we found that he was acutely sensitized in other tissues, as well as those of the nose and throat, to the toxic substance extracted from his teeth, and that the violent and frequent attacks entirely disappeared with the elimination of his dental infection. We are then, apparently dealing with a substance which obeys the classical expression of true anaphylaxis. If, however, sensitizations express themselves in a large variety of forms as we outlined in Chapter 30, and in

many, if not all, of which the dermal reaction is efficient in demonstrating them, why is it that individuals in perfectly normal health do not respond to dermal tests for sensitization and individuals with other forms of affections such as some of the rheumatic group lesions do respond to dermal reaction tests quite as effectively as those with the classical symptoms of sensitization, such as rhinitis, asthma, etc.? One of these two things obtains: either the classical rheumatic group lesions are in part forms of sensitization reactions, or there is a strange coincidence in these individuals' reacting contrary to the accepted significance of dermal reaction. To determine the presence in the body of an efficient defense for diphtheria, the Schick test is administered which is a dermal reaction test for that sensitization; similarly, the tuberculin test, the Abderhalden test, etc. We will discuss this further in the chapter on the mechanisms of local and systemic defense.

In Chapter 30, I discussed the fact that individuals may develop either or both a primary or secondary reaction to the skin test. The significance of these two and the mechanisms on which they are based are probably somewhat as follows: The first reaction seems to be a true allergy and consists of the reaction of the antibody with the antigen, and seems to be related only to the passage through the system of a toxin antigen produced by bacteria in some tissues of the body. This primary reaction frequently appears in thirty seconds; is unique in its characteristics, consisting of a central raised wheal surrounded by a zone of marked erythema, which frequently outlines the courses of the subdermal chains of lymphatics. It reaches its maximum usually in from fifteen to thirty minutes, and frequently within an hour is conspicuously disappearing, and may be quite lost in two hours. Occasionally this primary reaction may last three or four hours. In certain individuals there will appear at the site of this same test a secondary reaction beginning in from twelve to twenty-four hours. It may last from a few hours to several days, and in some instances there may be a considerable breaking down of the central zone. In the primary test there was a central white spot constituting the raised wheal. In the secondary reaction there is no raised central wheal, the erythematous zone extending from the center to the periphery, and most intense in the center.

The significance and nature of this secondary reaction is important. Whereas the primary reaction was dependent entirely

upon the presence in the system of a protein toxin without the presence of bacteria, the latter or secondary reaction seemed to indicate the presence in that system of the bacterium itself apart from, and in addition to, the toxins of the bacteria. We have, then, in the patients reacting only to primary sensitization evidence of a toxic irritation without bacterial invasion and in the latter evidence of a bacterial invasion. When both appear, both are present. When the second appears, it is our experience that, practically, always the primary is present. In the case referred to in Chapter 30, it will be noted that this patient was tested with three antigens, prepared in different ways, all of dental origin. This patient gave the primary reaction to all three of these antigens, but gave the secondary reaction to only one. We conclude, therefore, that he was suffering from a bacterial invasion of the body from the dental infection in addition to the toxin invasion. We have, then, by this procedure, what seems to be a means for determining whether an individual is suffering from either or both a toxic absorption from a focus or a bacterial invasion from it.

SUMMARY AND CONCLUSIONS.

This work that we are presenting here is, we consider, very important. But this shall be considered as a preliminary report as we are carrying forward these investigations and will have additional data to present later. These involve methods for the application of this principle in dental diagnosis and its application in making various determinations.

CHAPTER LII.

INTERPRETATIONS.

INTERPRETATION OF SEROLOGICAL STUDIES.

DISCUSSION.

In Chapters 19 and 20, I have presented researches conducted to determine something of the changes that are produced in various sera of the body by dental infections, in which we found some very marked results. For example, a patient suffering from hemophilia not only was relieved himself by having infected teeth removed (a most difficult process in his extreme condition for he was nearly dead from spontaneous hemorrhage chiefly from the gums but also from the nose, and was deaf in one ear from spontaneous hemorrhage in the internal ear), but cultures from these teeth, when inoculated into rabbits, produced similar changes, in many of which the clotting time was greatly lengthened and in several, spontaneous hemorrhages developed. One of these died in twenty hours with many spontaneous hemorrhages throughout its body, as shown in Chapter 60.

Similarly, we have seen marked secondary anemias rapidly improve after the removal of dental infections. (See Chapter 60 on Anemias.) So definite are these effects in some instances, that even the transfer of the infected teeth from the patient suffering from acute nephritis to a position beneath the skin of rabbits, has produced in several instances acute nephritis in the rabbits as shown in Figure 203. Not only can these conditions be produced by the introduction of the organisms, which have been grown from the infected teeth, but changes may be produced in the various sera by the introduction into the animal's body of the toxic substance extracted from teeth separated from the bacteria themselves. This is demonstrated in Chapter 17.

It seems to be proved that dental infections can be the chief causative factor in many of the disturbances which express themselves as changes (or in changes) of the various sera of the body. Whether or not these changes occur by direct reaction between the toxic substances developed by the teeth and the contents of the blood stream, either by disturbing the functioning of the glands of internal secretion, or as sensitization processes, either directly upon the vital fluids of the body or the tissues producing them, we are unable to state from the information available. It seems probable, however, that several of these forces are at work, and we must wait for much more research data before an interpretation can be made of these phenomena.

CHAPTER LIII.

INTERPRETATIONS.

THE RELATION OF GINGIVAL AND APICAL ABSORPTION TO SYSTEMIC DEFENSE.

DISCUSSION.

In Chapter 4, we studied the similarities and differences routinely expressing themselves in various individuals, which, in general, indicated that while individuals are not, in the main, comparable, the characteristics are sufficiently definite to use them as a basis for classification of those falling within different analagous groups.

In Chapter 3, we found that the local expressions of infection in bone about the teeth tended definitely for a classification of individuals into those with extensive absorption and those without. These differences were also found expressed in bone reactions in animals.

In Chapter 5, we discussed the gross relationships between local and systemic reactions and found not only that individuals can be classified according to these two methods of study, but that the classifications include not only, in general, individuals of the same groups, but the striking illustrations are the same individuals for each of the two sets of groupings. To illustrate: When we divided individuals into groups, selecting those who had the most extensive rarefaction about dental infections, and again made studies to determine the individuals that were without systemic expressions from dental infections, when such were present, our typical illustrations were the same particular individuals; and, similarly, when we selected the individuals with least reaction for a given dental infection, they proved to be the same individuals that we had selected as most strikingly significant of the group with marked susceptibility. Note that we said "*Least reaction for a given dental infection*" which is very different from saying individuals with the least infection. Considering these two conditions as representing extremes of local reaction on one hand, and systemic susceptibility on the other, we found that intermediate groups had similarly definite characteristics. Thus a lateral

tooth with a putrescent pulp would, in the individuals with absence of systemic susceptibility, be attended by very marked apical absorption and a fistula; in the individuals with low defense, very slight absorption and no fistula; and in the individuals with, ordinarily, a high defense but which defense has in recent time been broken by overload, there would be evidence of a zone of moderately extensive absorption, evidence of a healed fistula or none at all, or a zone of condensing osteitis surrounding the zone, made radiolucent by the rarefying osteitis.

In Chapter 8, we studied the relation of gingival infections to pulp infections and found that, in practically all cases of extensive gingival infection, the pulp is already involved, and in cases with moderate gingival infection, frequently so.

In Chapter 10, we studied the relation of gingival infection, or periodontoclasia, to systemic disturbance and found what seems to be an almost complete contradiction to the teaching and expectation of the professions, for instead of the dominance of gingival infections progressing in the order of systemic susceptibility, it tended, when considered in its acute forms, to be in precisely the reverse order, for, in separate studies compiled for me from my records by different members of my staff, the remarkable data came out that, in the cases of marked systemic susceptibility to rheumatic group lesions, practically no cases of acute periodontoclasia in the active stage were found; and, conversely, in the groups with high defense to rheumatic group lesions, frequently this type of disturbance was present. These are clearly brought out in Figures 85, 86, and 87 of that chapter.

In Chapter 11 we found by comparing gingival absorption with periapical absorption and tendency to caries, that with a given dental infection, let us say the amount that would be involved in putrescent pulps, the extent of the apical rarefaction tends to be in direct proportion to the susceptibility to gingival absorption to gingival irritants, clearly demonstrating a direct relationship. Not that either is causative to the other, but that each is a symptom or effect of the same causative factors.

In Chapter 12, we found that the extent of the absorption is rather a measure of the defense than a measure of the danger.

In Chapter 13, we found that the discharge from a dental fistula does not contain, ordinarily, large quantities of living organisms, as has been generally supposed, but contains very few, and such as are found are nearly all digested or phagocyted; that the discharge is made up almost entirely of blood plasma, leucocytes, and neutralized products.

In Chapters 45 to 56 inclusive, I have undertaken to interpret the phenomena in the light of this new information and have presented, for your consideration, that local reaction not only determines whether the patient is or is not relatively safe from his own focal dental infections, but also determines the physical conditions surrounding that dental infection as evidenced by the tissue changes.

If gingival absorption, and the same is true of apical, is, in large part, an effect of vigorous local reaction in Nature's effort to establish a quarantine and defend the patient, it should be possible for us to establish evidence that this reaction is definitely defensive in character. In Chapter 30, in our study of sensitization, we found that the toxic substance extracted from an infected tooth, in some instances prepares animals to be more violently attacked by the organisms grown from that tooth; that these animals were sensitized, as evidenced by dermal reactions, to both the toxic substance itself, if injected after six days, a true allergy, and to the toxin extracted from both the organisms and the artificial media in which they were grown. We also demonstrated patients sensitized acutely to their own dental infections in a variety of ways, one of which was accompanied by rhinitis, coryza, extreme headache, etc., which symptoms were entirely relieved by the removal of the infected teeth; and also that these patients have a very marked dermal reaction to the toxin extracted from their teeth.

We, therefore, may use this dermal reaction as a direct means for determining the presence or absence of this antigen in the tooth substance and in the product of the active local reaction: namely, the pus from the periodontoclasia pocket of that individual. To do this, we have made an extract of the toxin of the pus from the periodontoclasia pockets of the patient with very high defense whose roentgenograms are shown in Figure 262 of Chapter 46, and whose case is reported there in detail, and have found that whereas he did not have either a primary or secondary reaction to the toxic substance extracted from the pus taken from the periodontoclasia pockets, which was very abundant, he did have a definite reaction to the toxic substance extracted from the teeth, secured simply by breaking up the teeth and washing the pieces in a slightly alkaline fluid. The fluid about these teeth was also alkaline and the teeth were, as it were, steeped in it more effectively than by the process by which we made our extract. It is my interpretation at the present, that the blood plasma in

which these parts were so abundantly bathed carried an efficient supply of antibody to neutralize this antigen. While we do not yet understand the mechanisms of immunity, it seems very probable that there is significance in the fact that this patient's blood calcium is above the normal, which problem we are discussing in the next chapter.

This would seem to give an entirely new meaning to certain forms of gingival infections. Whereas we have in the past looked upon them as being evidences of a particular type of bacterial invasion or a bacterial invasion working in a tissue that is particularly prone to degeneration, the evidence now would lead us to conclude that there is inherent in the body, probably directly related to calcium metabolism, a mechanism of defense which adapts itself to tissues in all parts of the body, and which is a definite part of function of the hematogenous and lymphogenous circulations. In all tissues embarrassed by a threatened approach of bacterial invasion, there is, then, in these fluids, a force which manifests itself vigorously, and therefore efficiently, at the root apex. The problem is not unlike that at the gingival border except that there is no other means of escape for the bacterial and toxic substances than into the blood stream until Nature shall, by this activity, blaze a way to the surface as an apical fistula, and there, with a stream of neutralizing fluid, carry these invading products to zones outside of the body, for in this sense the alimentary tract is outside of the body and is so considered in biological studies, and this is Nature's quarantine. The price we pay for it is the destruction of alveolar bone, whether at the gingival margin or the apex, but it is abundantly worth the price. In succeeding chapters we will apply this interpretation to other types of infection.

This explains so many things that have been conundrums in the past. For example, why is it that the same condition, produced by a gold crown forced into the gingival tissue, will in one case produce so much absorption and inflammation, and in another the tissue makes little or no outcry against its presence? Or again, food is packed between teeth where the contact points have been lost. In one instance, the absorption of alveolar bone has taken place nearly to the apex; in another, the food is jammed against the tissues, week after week, with little or no local reaction. Not that the tissue is not injured and infected. It is, and that's the pity of it. Or again, why is it that in some mouths a

tooth with an infected pulp produces almost no local disturbance about the tooth, while in another if it does not have a fistula, it recurringly is very painful or tender? Apparently, in the light of these studies, in the latter case the reaction process is directly the measure of both the discomfort (which is incidental to the second) and a successful defense against systemic disturbance, while the tooth without this reaction not only is not painful but unlike the other, which will be easily extracted, it is very difficult to extract.

CHAPTER LIV.

INTERPRETATIONS.

THE RELATION OF LOCAL TISSUE REACTION TO CALCIUM METABOLISM.

DISCUSSION.

This is a problem regarding which there is very little in the literature; which does not mean that it is not very important but probably does indicate first, that it is a very difficult problem to study, and second, that it has not attained the prominence and importance that it seems destined to, in the studies of immunity and susceptibility.

In Chapter 19, we have studied serological changes in the blood produced by dental infections. In Chapters 19 and 20, we have discussed the marked changes in the various sera of the body, produced by dental infections. These have demonstrated that several of the factors involved seem very definitely to be related to calcium metabolism. For example, in Chapter 60, we have revealed a case where the patient was suffering from very acute hemophilia, which condition was greatly improved by the removal of his infected teeth, the cultures from which infected teeth, when inoculated into rabbits, not only produced striking changes in clotting time, but, in Chapter 60, there is shown a rabbit which bled to death from spontaneous internal hemorrhage within twenty hours after being inoculated with this strain, and there was not enough blood left in the heart and blood vessels to make a chemical analysis, which is frequently done. Similarly, the clotting time of many of these rabbits was delayed as was the patient's. This patient's total calcium was down to 8 mgs. where the ionic alone should be above 10.

In the various studies preceding this, we have been analyzing gradations in rarefaction of bone, both locally as a zone of absorption and a reduction of the total lime salts producing a radiolucency to the Roentgen-ray. These researches have shown that in most patients with a marked susceptibility or low defense, there is a marked increase in deposition of calcium, associated with condensing osteitis, and in individuals with a high resistance

and low susceptibility, there is a marked tendency to a reduction of osseous tissue with rarefying osteitis. In Chapter 34, in studying the effects of pregnancy, we found that during this period of calcium stress, as in the period of lactation, there is a marked susceptibility to rheumatic group lesions. The state of calcium hunger which obtains during periods of over-demand for calcium, as in pregnancy and lactation, seems clearly to be influenced and aggravated by the presence of streptococcal infection, such as dental infections.

The evidence at hand would seem to suggest that in most cases it is not so much the presence or absence of an available supply of calcium, such as calcium bearing foods, as it is a disturbance of the mechanism which governs calcium metabolism. In the subsequent chapters, in which we study in detail the individual cases, we have many instances suggesting a direct relationship between thyroid and parathyroid activity, and calcium metabolism and dental infection. That local tissue reaction is directly connected with calcium metabolism there seems no doubt. What this relationship is, and the means whereby local and systemic defense may be strengthened by modifying calcium metabolism, is not yet clear, but it is a problem of supreme importance and its study promises most favorable and important results for expended effort.

When we associate the relationships between the clinical conditions of the individuals and their ionic calcium, we find a very strong suggestion of relationships between cause and effect, and these are more strongly brought out when we review in connection with these clinical and chemical data, some of the determinations made *in vitro* and by animal experimentation with dental infections. Some of these are:

(a) *Individuals, with dental pathology of a type which expresses itself with liberal destruction of alveolar bone, whether at the gingival margin or at the apex, have at the time that process is active, generally, if not invariably, a normal or high ionic calcium of the blood; and, conversely, individuals, with a tendency to the development of deposition of calcium, as condensing osteitis, tend to have a low ionic calcium of the blood at the time that process is active.*

(b) *Individuals, with a marked tendency to dental caries, have at the time of the activity of that process, very generally, an ionic calcium of the blood below normal; and, conversely, individuals with complete freedom from caries almost without exception have an ionic calcium of the blood at or above normal.*

(c) *Individuals, with a low ionic calcium of the blood as a persisting and normal condition, tend to have much more dense and less permeable supporting structures for the teeth, as evidenced by the difficulty of producing anæsthesia; and, conversely, individuals with normally a high ionic calcium of the blood tend to have a condition of the supporting structures which makes them quite easily infiltrated with local anæsthetics.*

(d) *Individuals with a low ionic calcium of the blood tend to make a slow repair, with marked tendency to secondary infection of sockets following extraction; whereas, individuals with a high ionic calcium tend almost invariably to have a rapid repair, without tendency to secondary infection following extractions.*

(e) *The phenomena of the so-called dry socket, with its painful secondary infection following extraction, is almost exclusively limited to the individuals who, at the time or previously, and generally both, have a low ionic calcium of the blood.*

(f) *Radiopaque bones of various parts of the body tend to be associated with a chronic state of lowered ionic calcium of the blood; whereas, radiolucent bones tend to be associated with a high ionic calcium of the blood. The extreme forms of this which become pathologic, as osteomalacia, emphasize this same relationship.*

(g) *Individuals, with a low ionic calcium of the blood and with the consequent or associated condensing osteitis occurring about infected structures, tend to have the formation of sequestra; whereas individuals with a high ionic calcium rarely do so.*

(h) *Individuals with a high ionic calcium of the blood tend regularly to develop periodontoclasia and alveolitis as a reaction to local irritations; whereas, patients with a low ionic calcium do not tend to have this reaction.*

While it is exceedingly important that we shall visualize, even though imperfectly, somewhat of the role of calcium in metabolism and disturbed function, the problem is rendered doubly difficult by the fact, that incomplete statements, while in the main correct, will be read as complete statements; and I will ask that those who read this keep in mind continually that I am simply undertaking to associate the data that have been revealed in these researches and am suggesting what, in the light of the present knowledge, seems the most logical explanation. Some of these important relationships to be considered are:

(i) *When infected teeth are placed beneath the skins of rabbits, there is practically always a reduction of the ionic calcium of the cir-*

culating blood, which ionic calcium decreases progressively as death is approached, which generally occurs between six and seven milligrams.

(j) *When some infected teeth are placed in normal blood, this change in ionic calcium is rapidly produced.*

(k) *The pathologically combined factor can be determined and the bond with the toxic factor broken.*

We seem justified in suggesting the following as brief expressions of the role of calcium in life and metabolism:

1. Cellular function, whether hypo-, hyper-, or dis-function, is affected, if not directly controlled, by the concentration of ionic calcium in the bathing fluids.

2. Life in every form seems to be dependent upon free ionic calcium in the pabulum in which it exists.

3. The vital capacity and vital efficiency are both inseparable from, and dependent upon, calcium metabolism.

4. While the role of calcium in vital processes is of supreme importance, its presence or absence is probably not the primary and chief factor in cell function, since there are certain pathological states in which the calcium present is not of the order just stated, but one in quite direct confliction with these general principles.

CHAPTER LV.

INTERPRETATIONS.

THE MECHANISMS OF LOCAL AND SYSTEMIC DEFENSE.

DISCUSSION.

The science of immunology has not been developed far enough for the factors involved to be definitely segregated and interpreted. If we would undertake to summarize the eight preceding chapters and express the conclusions made in them in a generalization, it would be about as follows: Since I interpret local reaction to be the most important characteristic of local dental infection, and also that systemic defense against dental infections is a measure of ability of the system to establish an active local defense at the point of focal infection, together with an adequate defensive mechanism for each and every organ and tissue of the body, therefore immunity has, as one of its fundamental factors, a capacity for intracellular defensive reaction.

Our studies of the phenomena of sensitization, as applied to this problem, indicate that this condition plays a very large part in both a successful defense against dental infection and a sensitization to products of dental infection origin; and, also, that there is a direct relationship between anaphylaxis to dental infection and immunity against dental infection. Not that these are similar, but that they are closely related factors. Indeed, it seems probable, that in a very important degree or manner the disturbance which we recognize in one individual as a true type of allergy, with rhinitis, coryza, etc., is not unlike, except in manifestation and involved tissue, the reaction in synovial membranes, heart valves, kidney, etc. When antigen meets antibody, the reaction is intracellular. When the sensitized tissue, prepared for defense by its sensitization with its attached and occluded antibody, receives its arch enemy, the antigen which produced that sensitization, there is a violent local reaction with ischemia, hyperemia and distention, and often edema. If this reaction be violent enough, there is necrosis, which condition often follows our secondary reactions. A part of this process involves not only throwing into the tissue of the products of necrosis, but into

a tissue whose mechanism for repairing damage and removing waste has been disturbed or destroyed, either permanently or temporarily. We have, then, a localized necrotic process in an otherwise perfectly normal tissue.

Our studies have shown that the presence of the toxic substance taken from the teeth inoculated into animals frequently makes them more susceptible to attack by the organisms which produced that toxin. If, then, applying this to the local tissue, when the organism which produced the toxin is wandering through the system, having gone beyond the quarantine of the focal infection, where will it find its pabulum? It would seem most likely that it would be in tissue whose local defense has been destroyed by this *antigen antibody reaction* and which chemically and mechanically has been deprived of its local function for defense. There is also a pabulum of necrotic tissue for this organism; and the heart valve, synovial membrane, or kidney tissue becomes a prey to the dental infection. This may be only a theory, but we must have some visualization from which to start, and whether this be correct or incorrect, and there is much to suggest that it is largely true, it at least makes a starting point; and if this bridge across the chasm be not adequate to carry the entire responsibility of interpretation, it, at least, may serve as a temporary trestle until we can rebuild it with a more permanent structure.

In support of the hypothesis that I have just presented my researches have brought out among the important new data the following:

(1) Individuals with a high defense to the rheumatic group lesions seem, almost invariably, to have a high ionic calcium of the blood during and preceding that state of high defense.

(2) The ionic calcium of the blood seems definitely related to the capacity for reaction as expressed in the supporting structures of the teeth which have been injured by irritation, either gingival or apical.

(3) Individuals presenting with sensitization reactions of the type of allergies of the mucous membrane, skin, and special tissues, all have a high ionic calcium and a high pathologically combined calcium, and belong to the group which we would classify from the type of pathological changes in the injured supporting structures of the teeth, as having an acquired susceptibility.

(4) (a) Anaphylaxis from dental infections seems definitely to

be related either to a long continued state of reactivity, in which process certain tissues take on a hypersensitization; or (b) a reaction occurs as the result of the pathologically combined calcium or some other factor in a system whose normal defense is sufficiently high (and there is still available a normal ionic calcium in these cases) to prevent its expressing itself in joints and muscles and organ tissues, since these individuals with anaphylactic reactions to dental infections seem never to have the dental infection express itself as rheumatism, heart involvement, or neuritis, etc.

To state this last observation differently, if the systemic reaction to the pathologically combined calcium (assuming that the dental toxin is in combination, as our evidence seems to indicate, with a portion of the ionic calcium of the blood) occurs in an individual with high total calcium, or at least with a still sufficiently high ionic calcium to be practically normal, say 10 to 10.5 milligrams per 100 cc. of blood, the systemic reaction is liable to take the form of a sensitization which is similar to, if not identical with, the classical anaphylactic reactions of tissues to proteins. But if the reaction of the system is to a pathologically combined calcium which is definitely below the normal, that individual does not tend to have the classical anaphylactic symptoms, but does tend to have the usual rheumatic group lesions. There is evidence which strongly suggests that very many disturbances are modifications of anaphylactic reactions, for even those reactions taking place below the normal ionic calcium of the blood have many characteristics which, while they would be clearly distinguished from the classical anaphylactic group, do seem to be the result, in part, of sensitization processes in joints, muscle tissues, organ tissues, etc. Further, it now seems very probable that many of the reactions of the nervous system are in large part a type of sensitization reaction in those tissues, which may affect either motor or sensory groups or the central nervous system; and, indeed, the evidence strongly suggests that disturbed mental states, ranging from fear and discouragement or ordinary blues, insomnia, etc., on the one hand, to the serious mental disturbances such as dementia, mania, loss of memory, etc., may all be, in part, a type of sensitization reaction within the nervous system.

There is also evidence, as I have indicated in Chapter 31 on Dental Infections and Precancerous Conditions, that this state of exalted reaction to dental infection seems to be definitely related to chronic irritations such as erythemas, dermatoses, epi-

theliomata, warts, and moles, all of which are shown in the preceding and subsequent chapters to have definite relation, in some instances, to focal and dental infections, and completely and promptly disappear with the removal of the dental infections. I would therefore suggest as a possibility for consideration and for careful observation that, since cancer, for example, of the stomach tends to develop in the scars of old stomach ulcers, and since stomach ulcers are so definitely produced by strains having that elective localization when taken from teeth of patients suffering from stomach ulcer, and which disturbances in the patients in many instances, as shown, completely disappeared with removal of dental infections, and also since cancer is so distinctly on the increase, as are also focal dental infections, because far too many teeth are crowned, root-filled, and bridged, which teeth are thereby tied into the patients' mouths and cannot be exfoliated, nor have they their natural vent through the pulp canal, which, though not a safe safety valve, would do one of two things: either make the tooth so uncomfortable that it would have to be eliminated, or make an exit for the toxins of the tooth infections into the oral cavity instead of the patient's system: therefore, dental infections must be considered under suspicion of an indirect association with the causative factors of cancerous conditions. In support of this last observation I would call attention to the fact, that in our fourteen hundred more or less complete family histories, from which we have used approximately one-half as being sufficiently complete and dependable to be worthy of making deductions from, we have found that in the two groups, those with a distinct family rheumatic group tendency and those with a distinct high defense in the family, the appearance of cancer seems definitely to be in larger proportion in the group with natively a high defense and evidence of a break in that defense; in other words, an acquired susceptibility to rheumatic group lesions, which is the same group in which we have found, practically, all of our cases of anaphylaxis. May there not then be some direct relationship between these important facts? In other words, may it not be that the tendency to the development of cancer is directly related to that type of tissue reaction which, for want of a better classification, we are grouping as an anaphylactic reaction. As an illustration of this relationship, I would cite the following clinical case:

Case No. 1351.—A patient with a skin sensitization gave a history of five cases of death from cancer in the family, four on

one side of the ancestry. She, herself, was suffering from a heart lesion, from which her father had died and her mother was suffering. Following the extraction of an infected tooth, the reaction upon her heart was almost like an anaphylactic shock. Coming on some hours after the operation, it was therefore not related to the anæsthesia. It was, however, so profound as to make her bedridden, with much prostration, for approximately a week. Before and since that experience, while her mitral leakage places a limitation upon her activities, she has been able to carry on regular duties, and except for her limitation from overloads, leads a practically normal life. Unfortunately, this illustration carries, by inference, a suggestion that I am associating heart involvements with cancer. This is not my belief except as a sensitization process, which may be superimposed on an organic lesion, associates these in this individual.

I would, therefore, briefly summarize these relationships as follows:

1. Since the defensive mechanisms, which protect the tissues of individuals, reside primarily in the unit tissues of the body, hyperactivity of those mechanisms constitute phases of pathological states; and, in consequence, many of the acute involvements have their beginning in that state of hyperfunction.

2. Some of these processes are true antigen-antibody reactions, which antigen is of focal origin.

CHAPTER LVI.

INTERPRETATIONS.

NEW LIGHT ON THE PHENOMENA OF IMMUNITY AND SUSCEPTIBILITY TO DISTURBANCES FROM STREPTOCOCCAL INFECTIONS.

DISCUSSION.

The data developed by the various researches herewith reported, together with their application in about two thousand clinical cases reviewed in the succeeding chapters constituting Part Two, have completely changed my visualization of the phenomena of infection and immunity from dental infection sources. My interpretation had been based upon the fundamentals that I have presented as the problems for these various researches. A first change has come in my visualization of the role of the infecting organism. I now see it as a potential force, capable of adaptation through a range and to a degree entirely beyond my previous conceptions. When we inoculate either blood serum or the body lymph with a quantity of the mixed flora of the mouth, frequently no organisms will be found except streptococci and diplococci, with occasionally staphylococci, and these may require a slight modification or dilution of these sera; and, indeed, their growth will depend upon the relative volume of the inoculating dose and the health of the individual or animal.

As I now visualize it, every organ of the body furnishes to the blood stream some element or elements which constitute, or contribute to, the maintenance of the defense of that organ against invasion from these serophytic organisms, for they are practically the only organisms of those ordinarily contaminating the oral cavity, which can grow in these fluids. If any organ or tissue of the body become diseased and fail to furnish to the blood stream its quota of the defensive complex, the circulating media of the body—namely, the blood and lymph—will bring a defective defensive environment to the organism in any focus of that host's body. Their phenomenal capacity for adaptation seems to assist them in developing an attack for that defenseless tissue.

In this connection it must be remembered that an injured tissue or organ is not necessarily one with its defensive mechanism reduced, but is frequently one with its defensive mechanism called into play; and, consequently, the injuring of a tissue or organ in some part of the body will not necessarily call forth a localization in that tissue from a chronic focus; but, on the contrary, that hyperactive tissue has an abnormally high defense unless and until some of its tissue becomes hypo-active and necrotic.

But this state of diminished defense in some organ or tissue is not limited to the processes of degeneration, but it seems demonstrated that this quality, which constitutes a complete protection for a given organ or tissue, is an hereditary one; and, just as the eye may be developed without the brown pigment, so an organ may be developed without its complete defensive mechanism, probably some enzyme or other chemical elements. Consequently, in an individual, who by inheritance finds himself without his normal defense in any given organ or tissue, there is a predisposition for a focal infection, if it exist, to invade that apparently normal, but partially defenseless, tissue. Consequently, a very large number of individuals carry from birth the text of their death certificate, for the principal chapters of their life history of ill health and complaints are already determined, if not written. It is no accident that there are more deaths from heart in the families recorded in our case histories in 16 per cent of our studied cases than in the other 84 per cent. We must think of individuals continually in the light of their defensive mechanisms.

But defense spells reaction, and reaction battle, and battle the products of warfare. This completely changes my visualization of what takes place about the root of an infected tooth. Instead of the record's being one of quantity of soldiers on either side in the contest, since all the soldiery may be at rest, the local story is one of the nature of the combat. But we have known so little of that combat that we have continually mistaken effect for cause. It is not an accident that the strong man dies with typhoid fever or pneumonia, and the weaker man survives. The thing that has killed the former and not the latter, has been that his capacity for reaction has been so great and so suddenly developed that he has overwhelmed his own body with the products of that warfare. It is the patient with a high defense that is made violently sick with fever and prostration from an abscessed tooth; but he or she

is soon over it. The individual with low defense has neither the profound local disturbance about the tooth, with extensive swelling from acute dental infection, nor the profound systemic depression. A chronic infection in these two types of individuals will represent two quite different relationships between host and invader. In the individual with high defense, the invader is held at bay with a quarantine which is inviolable, which exists between the invader and the body of the host as a so-called granuloma and its highly vascular mechanism with defenses in excess of all possible attacking force that may be brought to bear by the invader. In the other individual, however, with the low defense, this tactful invader is able to live as a parasite on the pabulum furnished without calling forth antagonism and defensive activities of the host. In this state either or both the toxin or the bacterium may pass the sentries and reach various structures of the body, and in doing so succeed in developing degenerative and destructive processes.

In the history of warfare between units of people, it is always the practice to overwhelm and destroy the defensive mechanisms, such as forts, ammunition trains, etc., as a first requisite for the plundering of the conquered. What could be more subtle than the devices that we have shown to be used by the organisms in dental infections? They reside in a blockhouse within the domain of the invaded host. The boundary, which separates the non-vital dentin of a pulpless tooth from the vital cementum, is virtually an impassable barrier to both the bacteria within the tooth and the mechanisms of defense of the host. There is only one kind of patient that can ever destroy the organisms in the infected tooth, and these I have shown to be only those who have so high a vital capacity that they can carry their immunizing line of defense right up to the tooth and, while combating its toxic substances, proceed piece by piece to take the tooth down by a process of absorption, and, in taking it away, uncover and annihilate the various invaders that are seeking to destroy it.

But that is not all. While this boundary is an impassable barrier to both the bacteria and the defensive mechanisms of the host, our researches have shown that it is a permeable membrane which permits nutrition to pass to the organisms in their protected position. It is as though a den of desperadoes were supplied pipe lines and conduits, carrying into their impenetrable fortress a continuous supply of bread, butter, and meat, and all the requisites for a most vigorous life cycle.

But even this is not the most tragic phase of the combat. From this protected position these organisms may furnish, and seem inevitably to furnish, to every individual who does not maintain that adequate and supreme defense, a toxic substance which paralyzes the very soldiery with which the defense is maintained. In Chapter 41, Variations in the Defensive Factors of the Blood, and in Chapter 17, Quantity, Systemic Effect, and Tooth Capacity, and in Chapter 18, Studies of Pulpless Teeth, I have shown that the leucocytes are the fundamental defensive mechanism of the body and that they may be paralyzed so completely as to be incapable of function, by toxic substances given off by infected teeth, without the presence of apparently a single organism within the system; and, further, that every individual carries an index, which is available for reading, as to what his or her factor of safety is against streptococcal infection, for just as a study may be made of an army to determine its number of soldiers, the number of guns, the efficiency of its marksmen, and the reserve supply, just so the various defenses of any individual's body may be determined in quite general terms by a study of the defensive capacity and mechanisms of that individual's sera.

When a dental infection or any other infection develops within the body of an individual with high defense, the process, as I see it now, is about as follows: A few wandering streptococci will reach the body fluids, whether the blood, its serum, the lymph, or the cellular elements of various tissues. The first combat is largely a quantitative and mass action process. If the total infection be large, local tissue, whether body fluids or organized structure, may be overwhelmed, or the trauma which introduces the infection may destroy and devitalize tissue. If, however, the quantity has been small, the individual with a high defense will very clearly stamp out that infection in a very short time. When a few living streptococci are placed in normal blood, the chances for their proliferating are very small, for the factor of safety of a normal individual is relatively very high. If it had not been so, few of us would have survived any of ten thousand battles which have occured within our bodies.

But each individual has a first line defensive mechanism which corresponds with a police duty, ample to take care of individual ruffians or intruders. When, however, a rebellious mob attacks the community, the state militia is called out, which, however, is a reaction of the community that occurs only in the presence of

a serious invasion of the community's rights; and if, perchance, the violent invaders of the law cannot be subjected by the state militia, the national army will be called into service. But just as the state militia will not be called upon until the state peace is endangered, just so the national army will not be called upon until the national peace is endangered, or until the defensive process gets beyond the capacity of the smaller unit of defense. The circulating blood and lymph have an adequate defense for taking care of a few invading organisms; and if they should get past a first line defense, every tissue of the body has a defense against them as well as its own reserve. A small infection will not call forth a large defensive reaction any more than a single burglar will call forth the state militia. There must be a riot call for the secondary defense; and when the blood serum and body lymph cannot combat the infection, a system with an adequate defensive organization will so signal through the nerves and chemotactic mechanisms that the reserves will be called out.

Just here we come to one of the most fundamental of the processes. The reserves of the body are carried in circulating glands which are passing to every tissue of the body, carrying what we might think of as fire extinguishers, not used until the occasion demands. These circulating glands are the leucocytes. They are, perhaps, Nature's most wonderful mechanisms, for the list of accessories they furnish is large. Within one minute after living or dead organisms are placed in normal blood, whether circulating in the body or out in the test tube, their presence in the blood will call forth from these leucocytes, chemicals which will destroy those invading organisms in very large numbers. They are the state militia, but unlike the state militia are omnipresent, being ready for a riot call at any place at any time.

But just here comes the great difference between the various individuals that make up society. Whereas some individuals furnish a blood plasma that will kill quite a large number of organisms without calling upon the reserve forces of the leucocytes, other individuals have a very low capacity for killing; in other words, there is a very low bactericidal property to the blood serum and the lymph. This is clearly shown by heating the blood of those individuals, when drawn, to 48°C., which, as Wright has shown, kills the leucocytes and leaves the blood only its police force without the privilege of calling upon its state militia, to use our simile. With some individuals the calling forth of

this secondary defensive mechanism will be accomplished with a very slight invasion. These are the people who, when they have a cold or Flu, have it sharply for a day or two and they are over it; or if they have an abscessed tooth, it swells violently and there is a profuse discharge, they have a high temperature, are greatly prostrated for a short period, but are over it quickly. Their prostration is in a sense a measure of the promptness of their reaction and the completeness and speediness with which they have split the foreign protein, which, incidentally, is momentarily poisoning their whole system until it is eliminated.

We have thought of the defensive mechanism of the leucocytes largely in terms of their capacity to phagocyte. I have shown in Chapter 41, Variations in the Defensive Factors of the Blood, as have also others, that the blood of a normal individual will devitalize a vigorous vital culture so that but a small fraction, in many instances, of the total quantity of organisms will grow after being subjected to that blood for the small space of time of one minute; whereas, if this blood were heated to 48°C. for one minute, which would kill the leucocytes, very few of the organisms would be destroyed.

Another and most important phase is the following: We think of defensive reactions as we do chemical reactions, that a small defense will take care of a few organisms; and if more organisms shall invade the blood stream, results will always be a measure of the defensive capacity; in other words, that defense is always quantitative in its relation to invasion. But Wright has shown that this is not the case, which facts we have verified in our work. With small doses of infection applied to blood *in vitro*, a very low percentage of these organisms may be devitalized; whereas, in that same blood, it may be that the addition of a larger dose will increase the reactivity from, let us say, a few per cent less than 10 in the first instance to over 99 per cent with the larger dose. (See the illustration in Figure 248.) In that case it will be seen that after inoculation of the blood with one thousand dead organisms for twenty minutes, it was able to destroy approximately 99 per cent of a thousand live ones which were exposed to it for only ten minutes and then placed in culture media. This is one of the most marvelous illustrations of chemotactic reaction that we know of in all biology; and it is most striking that this very difference is just as clear cut when the test is applied to the blood of our patients with a defective or deficient defense. Such a con-

dition is shown in Figure 248. This, then, becomes not only a means for determining quite rapidly the measure of the patient's capacity for defending himself or herself against dental infections, but also gives a means for determining whether a vaccine made of these dead organisms will be helpful to that patient and in what dosage the vaccine will be most helpful. I have shown in the figures of that chapter the relative efficiency of vaccines made by different methods. If the blood of a given individual reveals, on making these, that the donor does not have within the blood even a capacity for reaction, regardless of the size of the vaccinating dose, the process of vaccination can only be harmful; and this in all probability explains why such variable results have been obtained by the use of vaccines. In my own hands I have had most discouraging results in some cases and most encouraging in others. Many of each of these will be referred to in the succeeding chapters.

For those individuals who do not have a capacity for rallying a depressed defensive reaction, the prognosis is very bad. Whether this condition is the result of a vicious cycle set up by the organisms is not clear. There is a strong suggestion, however, that it relates both to type of organism and to type of defense. These are the individuals who frequently have recurring rheumatic group attacks, very often involving the heart, and from which they never entirely recover though at times seeming relatively free. When in the attacks, the streptococci can nearly always be grown from their blood. The question as to how long this state will exist and whether they will some day regain a defense is problematic. For many of them the prognosis must be guarded and the condition considered serious, if not grave. But just here we see the need for intensive research on an adequately comprehensive scale to develop a chemotactic means for supplying to these patients what they do not already possess or the mechanisms to create. For some, blood transfusions will be helpful, but usually temporarily so, if the state is a chronic one. The data I am developing on this phase of the problem is not ready for presentation but will be presented in a separate communication.

In the succeeding chapters of this book, constituting the second part, I will review case histories and clinical data relating to a large number of groups of affections which more or less frequently disturb humanity. Unfortunately, the prevalence of these disturbances is very much greater and the incidence very much more

suttle and of longer standing than has been anticipated. I have spoken of these as the *rheumatic group lesions*. It seems probable that we will come more and more to speak of them as the *degenerative diseases*, since they constitute the slow loss of function, with structural degeneration, of various organs and tissues of the body. The government statistics speak of them frequently as *old age diseases*, and it is pathetic that so many individuals are slowly dying of old age diseases anywhere from thirty years on.

But this raises the question as to the etiology of these old age or degenerative diseases. We have thought of endocarditis, nephritis, cholecystitis, etc., particularly the first, as being the result of an accidental invasion of the body by an organism which has attacked the heart or other involved tissue, or, perchance, that the individual was born with a defective heart. It is most tragic that, whereas the death rate has been reduced in the acute infectious diseases, it not only has not been decreased in the degenerative diseases but in some instances and communities seems definitely to be on the increase. If the placing of an infected tooth beneath the skin of a rabbit can in weeks, months, or a year, (illustrations of which we have produced), develop a typical nephritis in a rabbit where the tooth was taken from a patient suffering from nephritis, (we have evidence indicating that the teeth of individuals without apparent nephritis may also produce nephritis in rabbits, though not in so large per cent,) it then becomes a matter of great concern and responsibility that in those communities and in the groups of individuals with most focal dental infections, the incidence of these degenerative diseases is greatest. Perhaps no lesson of greater import to the health of the nation has come out of these various studies than the fact, that in our hundreds of carefully taken case histories, as shown in Chapter 4, incidence of these degenerative diseases is many fold greater in those individuals with known focal dental infection than those known to be free from dental infection. I am not presuming that these may not be associated factors in part, but I am satisfied that they are, in addition, contributing factors, the latter to the former.

I will, therefore, urge that the members of the dental profession will keep this thought in mind as they review the many cases of degenerative diseases presented in the subsequent chapters and that they shall note the large number of instances in which even so severe conditions as critical heart involvements have quite completely subsided and remained quiescent for years by the

removal of dental focal infection, and also the high incidence in which the infection from these dental infections produced comparable lesions in experimental animals; and, as you read, I beg of you to keep in mind and note critically how almost invariably the dental focal infection existed about a tooth which was entirely comfortable and from the old standards of valuation was efficient and safe, notwithstanding its demonstrated potential capacity for harm. I also beg permission to suggest to physicians, who will read this, that they recognize first that teeth may have an almost incalculable value either for mastication or the retention of mechanisms for mastication, and it is a harm that can scarcely be estimated to remove teeth that are not injuring the individual, for in many instances we have seen individuals doomed to two crutches instead of one, by making them dental cripples without doing the slightest benefit to their dental conditions, or for lack of an adequate interpretation and diagnosis.

There is a phase of the process of immunity which we have but little understood, namely the injurious effects resulting from long maintained defensive reaction. We can readily understand, for example, how the persistent use of water to prevent combustion would probably introduce injurious disturbances of an entirely different kind than those we are seeking to combat. We have seen how the very process by which nature tends to neutralize imperfectly reduced acid products, may deplete the body of bases essential for organ tissue functioning, such for example as calcium, thereby depleting the tissues of the ionic calcium required for metabolic processes. The development of these acid products may be produced by many individual or combined forces, a very important one being improper food intake. There is, however, a role in which dental infections enter very directly into this problem, for, as we have demonstrated, the placing of an infected tooth beneath the skin of a rabbit may act very directly upon the acid-base balance of the animal. In the succeeding chapters in Volume Two we will see many cases where the alkalinity index progressed rapidly toward normal with the removal of dental infections. Few, if any, of the forces producing disturbed function and organ and tissue degeneration, are so important as are the forces disturbing the acid-base balance. I have shown that when rabbits are chilled for a few minutes in ice water they will develop suppurative arthritis from an inoculation of dental infection so small as to produce practically

no effect on the control animals not chilled. The chilling of these animals disturbs the local circulation, thus preventing a normal drainage from the tissues of the acid products of catabolism, which should normally be transported regularly and rapidly through the blood, carried by the erythrocytes and discharged largely through the lungs as carbon dioxide. One can get a simple demonstration of the small amount of retained acid products that will do harm, the oxidation of which is accomplished by the inhaled oxygen, by ceasing to breathe for a few minutes and noting the distress. This is just as true of any isolated tissue as when it involves the entire organism. The war experience has demonstrated that the compression of blood vessels by the placing of tourniquets, caused the accumulation in that limb, in which the circulation was cut off, of acid products which depleted the alkali reserve of not only those tissues, but also of the entire body, when the circulation was re-established, resulting in profound and often fatal shock from acidosis. Indeed it now seems demonstrated that shock is largely, if not chiefly, the result of such disturbances in the acid-base relationships. When these processes develop slowly, there is a distinctly different type of disturbance. The individual suffers a sense of depression and lassitude characterized by special organ disfunctions, which disfunctions are fundamentally due to organ and tissue change, the extent of which is the measure of organ and tissue degeneration. If, as seems indicated if not demonstrated, infected teeth carry toxic substances capable of directly disturbing the acid-base balance by means of a substance or substances in many respects resembling guanidin, they are potentially of prime importance in the production of organ and tissue disfunctions, degeneration, and chronic shock.

Dental infections are thereby of double importance since they play this dual role, for in addition to this direct effect upon the blood, they produce acute and chronic changes in blood vessel walls often resulting in their spontaneous perforation, and develop bacterial invasions with local necrosis. In short, we find an infected dental tooth to be an enemy fortress within the tissues of the host from which, by these various processes, the invading organisms may break down with progressive degenerative processes various of the organs and the tissues of the body, while the host is virtually helpless to defend itself because of their insidious methods of warfare.

The detailed study of a large number of typical and illustrative cases with special references to their clinical aspects, will constitute the second part of this presentation, which is placed under a separate cover as Volume Two. This division of the work into two units has become necessary owing to the difficulty of handling so large a volume.

I will, accordingly, summarize the phenomena of immunity and susceptibility from streptococcal infections briefly as follows:

1. Dental infections are essentially battle grounds between protected invading streptococcal infections and a more or less efficiently reacting host. The capacity for reaction on the part of the host determines the appearance of the battle ground in the local zone and the depredations of the sneaking invaders in the systemic zones.

2. The capacities of the host for making an adequate warfare are determinable qualities relating to the body fluids, chiefly to the blood.

3. The degenerative diseases have their origin in part, and I fear in quite large part, in dental focal infections.

3. The most important step that can be taken for the still greater improvement of the health of the nation can, in my belief, be had in the systematic prevention of focal infections, of which the dental group constitutes by far the largest proportion.

CHAPTER LVII.

GENERAL SUMMARY AND RESTATEMENT OF FUNDAMENTALS.

INTRODUCTION.

If my interpretations of the preceding researches are correct, there is need for a recasting of the fundamentals for diagnosis, prognosis, and treatment; and I am not unmindful of the tremendous responsibility that I am assuming in suggesting a new alignment of these fundamental principles. It has been because of a recognition of this tremendous responsibility that I have refrained from publishing these data until after I have had a chance to test them out on not a few hundred but on many hundreds of cases, and my presumption and my final willingness to do so are based entirely upon my personal confidence that they are correct. I do not assume that my interpretations are in every detail as later information will indicate, but in the light of present knowledge, they seem to me to be the most logical, and I feel it my duty to give them to humanity and the professions in order that others may assist me in correcting and enlarging them as further facts may indicate. I hope to have an opportunity to strengthen or reinterpret with the addition of new data which I am rapidly accumulating. I have no interest or desire that these suggestions shall prevail, except as they may be found to be based upon truth, and he will be my most kind friend who will furnish data to establish their incorrectness.

I have, accordingly, for simplicity and clearness undertaken to make a brief statement of the old, or generally accepted, interpretations and have placed these in one column, and have placed in a parallel column what I would deem to be a more nearly correct interpretation in the light of the available data. I do not presume that all members of the profession are at present interpreting these fundamentals as I am wording them in the old viewpoint. I believe, however, that the great majority of the members of the healing professions do so interpret; and no one will be more glad than myself if I be in error in this conviction. The following is a statement of the old and the new interpretations as I have suggested them.

The preceding research problems cover the fundamentals that have been in general consideration in problems of dental diagnosis, prognosis, and treatment. My researches upon them have opened up many additional problems, twenty-seven of which I have presented in the latter part of the preceding chapters. There cannot, therefore, be given for these latter problems, an old and a new interpretation. I will, accordingly, present herewith, some general interpretations growing out of the general applications and later researches, and in place of the statement of the problem as an old fundamental in the left hand column as in the first seventeen chapters, will simply state the problem.

OLD INTERPRETATIONS	NEW INTERPRETATIONS
NO. 1. ROENTGEN-RAY LIMITATIONS.	
(a) Roentgenograms of teeth will reveal the presence of infection. *(b) The apparent extent of the absorption is the extent of the infection.* *(c) An area of absorption, if present, can be disclosed by the roentgenogram.*	**(a) Roentgenograms do not reveal infection, and may or may not reveal its effects.** **(b) The extent of the absorption does not express the extent of the infection, except in part as that individual's reaction to the infection is understood.** **(c) An area of absorption of the supporting tissue at the apex of a tooth, or laterally, may not be disclosed because of any of the following conditions: (1) Being hidden by a part of that tooth, such as another root; (2) A heavy mass of bone, such as the malar bone; (3) A layer of condensing osteitis obscuring the rarefying osteitis.**
NO. 2. BACTERIAL CAUSE.	
If dental infections produce disturbance in other parts of the body, it is because the organism that has chanced to invade that tissue is one having the specific qualities for that invasion and localization regardless of the host, much as the organisms of erysipelas and mumps will respectively select the skin and parotid gland.	**Dental infections involving root canals and their apices and supporting structures practically always contain streptococci, of which, biologically, there are many types or strains, any one of which may be the important causative factor for any of the various types of rheumatic group lesions, regardless of biological classification. The elective localization and attacking qualities are developed by the environment and are, consequently, a factor of the soil or host.**

OLD INTERPRETATIONS	NEW INTERPRETATIONS
NO. 3. LOCAL ORAL STRUCTURAL CHANGES.	
(a) Dental infection in bone will express itself as absorption. *(b) A given dental infection will express itself in the local tissues of the mouth approximately the same in all people.*	(a) Dental infection in bone may express itself as absorption, even extensive absorption, or may be attended by very little or no absorption, or may even produce a marked increase in the density of the bone. (b) A given dental infection will not express itself in the local tissues of the mouth approximately the same in all people. People tend to divide into groups with regard to this matter of local reaction, which groups are very dissimilar.
NO. 4. SYSTEMIC REACTIONS. ARE HUMAN BEINGS COMPARABLE?	
Human beings are similar in their susceptibility to reactions to dental infections, or sufficiently so, that they may be considered comparable and be judged by the same standards.	Human beings do not react with sufficiently uniform similarity to justify the premise that they can all be judged by the same standards and, therefore, may be considered comparable in their susceptibility to systemic involvement from dental infections. They can, however, be divided into groups, the members of which are sufficiently similar to be judged by the same general standards, and they of that group may, therefore, be considered comparable. On the basis of this quality of susceptibility, they readily classify into three groups: namely, those with an inherited susceptibility, those with an acquired susceptibility, and those without a susceptibility to rheumatic group lesions.
NO. 5. RELATIONSHIPS BETWEEN LOCAL AND SYSTEMIC EXPRESSIONS.	
Since, according to the presumption all individuals are similar, and since dental infections are entirely dependent for their characteristics upon the type of organism which has chanced to secure access, therefore there are no characteristics of the local tissue pathology which are related to the degree of susceptibility or nature of systemic involvement.	Local dental pathology about an infected tooth has variations which make grouping and classification easily possible on this basis, which groups have a direct relationship with similar groupings that can be made on the basis of susceptibility to rheumatic group lesions. The local and systemic expressions are not only related, but are both symptoms of the same controlling forces and conditions.

OLD INTERPRETATIONS	NEW INTERPRETATIONS
NO. 6. VISIBLE ABSORPTION AND TOOTH INFECTION.	
(a) A tooth without visible absorption at its apex is not infected. *(b) A tooth with visible absorption at its apex is infected.*	(a) Teeth without absorption at their apices can be, and frequently are, infected in the pulp, dentin, and apical tissue. (b) Teeth with periapical absorption can have the same produced by irritating medication or trauma.
NO. 7. CARIES AND PULP INFECTION.	
Pulps of teeth not exposed by caries are not infected.	Teeth with moderate caries frequently and with deep caries generally, have their pulps already infected to some extent through this channel.
NO. 8. PERIODONTOCLASIA AND PULP INFECTION.	
Pulps of teeth with pockets from periodontoclasia not involving the apex are not infected.	Teeth with shallow or moderate pockets from periodontoclasia frequently, and with deep pockets from periodontoclasia usually, have their pulps already infected to some extent from that source.
NO. 9. CARIES AND SYSTEMIC INVOLVEMENT.	
There is no relationship between caries and systemic involvements.	Susceptibility to dental caries and systemic involvements from dental lesions are proportional, both as cause and effect and as related symptoms.
NO. 10. PERIODONTOCLASIA AND SYSTEMIC INVOLVEMENT.	
With an increase of susceptibility to periodontoclasia, there is a marked increase in susceptibility to rheumatic group lesions.	Individuals with marked susceptibility to periodontoclasia have, as a group, a decreased susceptibility to the rheumatic group lesions during the period of its active development (in its secondary stages it may contribute to rheumatic group lesions;) or expressed otherwise, individuals with a very marked susceptibility to rheumatic group lesions tend, in general, to be free from extensive periodontoclasia; and when rheumatic susceptibility does develop, it would generally be classed as an acquired factor.

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NO. 11. PERIODONTAL AND APICAL REACTIONS.

There is no relationship between the extent of apical absorption from a pulp involvement and the presence or absence of a periodontal absorption from a gingival irritation.

There is a direct relationship between tendency to absorption of alveolar bone in response to irritation, whether at the gingival border or at the root apex; and individuals with extensive periodontoclasia have, for a given dental infection, much more extensive areas of absorption at the apices of infected roots, than do patients without a tendency to periodontoclasia.

NO. 12. RELATION OF APICAL ABSORPTION TO DANGER.

The quantity or extent of the absorption is a measure of the danger; or otherwise expressed, the size or extent of the disclosed area of absorption at the apex of the root of a tooth is directly an expression of the quantity of infection and, therefore, a measure of the danger from it.

Since different people react differently, through a wide range, to a given infection, the extent of the area of absorption is not a measure of the danger; but, on the contrary, it may be, and frequently is true that the patient suffering severely from a systemic reaction caused by a dental infection shows very little absorption compared with that which the same dental infection would produce in a patient with ample and high resistance.

NO. 13. NATURE OF FISTULA DISCHARGE.

Flowing pus from a fistula is, necessarily, very dangerous to the patient since it is an expression of the quantity of local infection and, therefore, a measure of the danger from it.

Since an adequately active defense against a dental infection, both locally and systemically, produces a vigorous local reaction with attending extensive absorption and the products of inflammatory reaction, namely, exudate and plasma in sufficient quantity to require an overflow, usually spoken of as pus from a fistula, this overflow may be, and usually is, evidence of an active defense and is constituted almost wholly of neutralized products and is often sterile, and such a condition is much more safe than the same infected tooth without such an active local reaction.

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NO. 14. ROOT CANAL MEDICATIONS.

(a) Infected teeth can be sterilized readily by medication.

(b) Usual medications do not injure the supporting structure.

(a) Infected teeth can be completely sterilized in the mouth only with great difficulty, or by the use of medicaments whose irritability readily injures the vitality of the supporting structures of the teeth.

(b) Many of the usual methods used for the sterilization of infected teeth do serious injury to the supporting structures about the teeth.

NO. 15. ROOT CANAL FILLINGS.

Root fillings fill pulp canals and continue to do so.

Root fillings rarely fill pulp canals sufficiently, perfectly to shut out bacteria, completely or permanently. Root fillings usually fill the pulp canal much less perfectly some time after the operation, than at the time of the operation, due to the contraction of the root-filling material. The ultimate volume contraction of the root filling is approximately the amount of solvent used where a solvent is used with gutta-percha as a root-filling material. Infection is a relative matter, and quantity and danger are both related to defense, which defense may vary from high to exceedingly low.

NO. 16. COMFORT AS A SYMPTOM.

Local comfort and efficiency of treated teeth are an evidence and measure of the success of an operation.

Local comfort not only is not a certain index of success or safety, but may constitute both what is probably one of the greatest paradoxes and one of the costliest diagnostic mistakes through injury to health, that exists in both dental and medical practice, because it may only mean the absence of local reaction which would, if present, incidentally make the tooth sore and fundamentally destroy the infection at its source whereas, the absence of this local reaction and its consequent destruction of the infection products, permits them to pass throughout the body to irritate and break down that patient's most susceptible tissue, which tissue can be anticipated very frequently, if not generally.

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NO. 17. CAPACITY FOR INFECTION OF ROOT-FILLED TEETH.

When infected teeth produce disturbance in other parts of the body, it is primarily because the patient is overwhelmed by a large quantity of infection.

When infected teeth produce disturbance in other parts of the body, it is not necessary that the quantity of infection be large, nor is it demonstrated that it is necessary that organisms always pass throughout the body or to the special tissues involved, but the evidence at hand strongly suggests that soluble poisons may pass from the infected teeth to the lymph or blood circulation, or both, and produce systemic disturbances entirely out of proportion to the quantity of poison involved. The evidence indicates that this toxic substance may, under certain conditions, sensitize the body or special tissues, so that very small quantities of the toxin or of the organisms which produce it, may produce very marked reactions and disturbances in that tissue.

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NO. 18. STUDIES OF PULPLESS TEETH.

Have pulpless teeth injurious contents other than microörganisms?

Infected teeth may contain in addition to microörganisms toxic substances, which produce very profound effects upon experimental animals and which tend to prepare the tissues of the host, at least in some cases, for a more ready invasion by the organisms growing in that tooth.

NO. 19. HEMATOLOGICAL CHANGES IN THE BLOOD.

What changes are produced in the blood and sera of the body by dental infections?

Dental infections may produce very serious changes in the blood and sera of the body, some of the most frequent of which are leucopenia, erythropenia, lymphocytosis, and hemophilia.

NO. 20. CHEMICAL CHANGES OF THE BLOOD.

What are the chemical changes that are produced in the blood by acute and chronic dental focal infections?

Dental focal infections tend to produce, in many instances, one or several chemical changes in the blood, which changes tend also to be produced in animals when an infected tooth is placed beneath its skin, and, similarly, with certain methods of inoculation with the culture grown from these

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teeth. Some of the changes most frequently found involve:

(a) The ionic calcium of the blood.

(b) The presence of a pathologically combined quantity of calcium in the blood.

(c) A reduction of the alkali reserve of the blood.

(d) The development of acidosis.

(e) An increase in the blood sugar.

(f) An increase in the uric acid.

(g) The development of nitrogen retention.

(h) The development of products of imperfect oxidation.

NO. 21. CONTRIBUTING OVERLOADS WHICH MODIFY DEFENSIVE FACTORS.

What are the contributing factors causing a break in resistance?

Dental infections, while potentially harmful, may not be causing apparent or serious injury until the individual is subjected to some other overload, at which time a serious break may come. The chief contributing overloads are influenza, pregnancy, lactation, malnutrition, exposure, grief, worry, fear, heredity, and age.

NO. 22. ELECTIVE LOCALIZATION AND TISSUE AND ORGAN SUSCEPTIBILITY PHENOMENA.

Do the organisms of dental infections possess or acquire tissue affinity and elective localization qualities?

Dental infections may or may not contain organisms with a specific elective localization quality for certain tissues of the body. When they do so it is generally because the host is then suffering, or has previously suffered, from an acute process in that tissue, which acute process frequently, entirely and permanently, disappears with the removal of the focus of infection. There is evidence to indicate that the complete removal of an organ so affected does not destroy that elective localization quality in the microörganisms of the focus. Defense and absence of defense to streptococcal infection as an organ and tissue quality, seems definitely to be related to inheritance and, as such, obeys the laws of mendelian characteristics.

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NO. 23. ENVIRONMENT PRODUCED BY INFECTED PULPLESS TOOTH.

What are the characteristics of the habitat and environment furnished for bacteria in an infected pulpless tooth?

Since an infected tooth is a fortress for bacteria within the tissues of the host, and since, in accordance with the laws governing the behavior of solvents and solutes, the dissolved substances within the tooth can pass to the outside of it, and, similarly, the dissolved substances outside the tooth can pass to the inside of it, together with the fact that the defensive mechanisms of the body are quite unable to enter and reach the bacteria within the tooth except in exceedingly small numbers through the natural openings of the root, which openings will, however, permit the organisms to pass at will from within the tooth to the outside, we must conclude that an infected tooth furnishes a condition and environment that is tremendously in favor of the invading organism inhabiting it, as compared with the host, since the latter may only rid itself of the menace by exfoliating it or absorbing it.

NO. 24. ELECTIVE LOCALIZATION AND ORGAN DEFENSE.

Do diseased organs and tissues modify bacteria growing in the distant focus, or create in them a capacity for elective localization for those diseased tissues?

We are led to conclude from the available data, that we do not as yet have sufficient information to draw a close distinction between the influences of the organisms on the affected organ, in contradistinction to the influences of the diseased organ upon the organisms in the focus. The available data suggest strongly, if they do not definitely indicate, that both these conditions exist, in some instances, either one acting entirely alone, and in some others there are indications that both exist at the same time.

NO. 25. RELATION OF IRRITANT TO TYPE OF REACTION.

Have we different products from dental infection?

The evidence available indicates that infected teeth elaborate two distinctly different products, one being bacteria, and the other a toxic substance or group of

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toxic substances, which, independently of the organisms developing them, may produce various and profound disturbances in tissues in various parts of the body, one of the important group of disturbances being that of the blood stream.

NO. 26. CHEMOTAXIS AS A MEANS FOR INCREASING DEFENSE.

Can defense for streptococcal infections be increased by introducing enterally or parenterally (by ingesting or injecting) chemicals?

These preliminary experiments would seem to suggest that, means can be developed which will effectually assist, by chemical means in the defense of the body against the invading streptococcal organisms of dental origin or from other sources which produce the rheumatic group lesions.

NO. 27. THE EFFECT OF RADIATION ON DENTAL PATHOLOGICAL LESIONS.

Can periodontoclasia and apical abscess and inflammation be cured by various types of radiation?

(a) These three forms of radiation—namely, Roentgen-ray, radium radiation, and ultraviolet as generated from mercury vapor and quartz tube—have definite effect on cell resistance and proliferation, and thus directly upon tissue reaction expressions such as pus, bacterial invasion, and granulation.

(b) Some of these forces are apparently definitely harmful; others are apparently definitely helpful.

NO. 28. GINGIVAL INFECTIONS, THEIR PATHOLOGY AND SIGNIFICANCE.

Are the present theories regarding the etiology of periodontoclasia, or so-called pyorrhea alveolaris, correct?

(a) Inflammatory processes of the tissues about the teeth are a direct expression, and therefore a measure of the vital capacity for reaction of that individual to an irritant, during those stages of these lesions, characterized by an abnormally high vital reaction.

(b) The individual, who has had this capacity for a very active reaction to the presence of irritants, may pass into a condition or state in which he or she has lost that high defensive factor, at which time sev-

eral changes develop, including a cessation of the absorption of alveolar bone, a lowering of the alkalinity of the periodontoclasia pockets, a change in their bacterial flora, all of which may provide under these later conditions a focus for systemic infection of the most dangerous type, though they may have ceased to have evidence either of local inflammatory disturbance, or exudate as pus.

(c) To the ordinary observer, lay or professional, these two very dissimilar states are considered to be similar or identical though they are potentially very different.

(d) These different peridental expressions or reactions to irritations are accompanied by, and doubtless related to, changes in the ionic calcium and alkali reserve of the blood.

NO. 29. ETIOLOGICAL FACTORS IN DENTAL CARIES.

What are the dominant etiological factors in dental caries?

Dental caries is dependent upon the following factors:

(a) A reduction in the hydrogen ion concentration of the normal environment of the tooth.

(b) An acid producing bacterium.

(c) A change in the chemical constituents of the pabulum bathing the tooth.

NO. 30. THE NATURE OF SENSITIZATION REACTIONS.

Do dental infections produce sensitizations of an anaphylactic character?

(a) Teeth contain substances other than bacteria to which the individual may become sensitized, and which substances may, in addition, have strong toxic properties.

(b) The evidence here presented suggests that dental infections are capable of producing in an individual a state of anaphylactic sensitization, which condition may entirely and apparently permanently disappear with the removal of the dental infections. These disturbances may occur in dermal tissues, mucous membranes of the nose and throat, lacrimal tissues, mucous membranes of the bronchioles and air passages, as asthma, and the mucous mem-

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branes of the digestive tract and a number of other types of tissues.

NO. 31. PRECANCEROUS SKIN IRRITATIONS.

Are there relationships between precancerous skin irritations and dental infections?

The evidence available suggests:

(a) That dental infections may produce localized anaphylactic reactions, as irritations of the skin and mucous membranes.

(b) That these sensitizations may develop into precancerous conditions.

NO. 32. DENTAL INFECTIONS AND CARBOHYDRATE METABOLISM.

What, if any, is the relationship between dental infections and carbohydrate metabolism?

Dental infections may produce marked changes in carbohydrate metabolism and probably structural and degenerative changes in the islets of Langerhans of the pancreas, with the production of hyperglycemia and glycosuria.

NO. 33. MARASMUS.

Why do people with rheumatic group lesions tend to be underweight?

Dental infections, when they affect the patient systemically, frequently, if not generally, produce a depression of the individual's weight; and marasmus, whether mild or severe, may be considered one of the diagnostic symptoms in studying the relation of dental infections to general health.

NO. 34. PREGNANCY COMPLICATIONS.

Do dental infections have a bearing on pregnancy complications?

(a) These researches have shown that in animals, infections from dental origin may have a very far-reaching effect on each the expectant mother and her fetus, which latter may be prematurely expelled or may be rendered lifeless.

(b) Inasmuch as a large number of our serious cases of rheumatism, heart, and kidney involvements, have their origin at the time of pregnancy in humans, in which cases our clinical histories show that there have been present extensive dental focal infections, it is suggested as important, if not improbable, that expectant mothers shall be free from dental focal infections, both for their own safety and efficiency and for the continued vitality of the fetus.

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NO. 35. SPIROCHETE AND AMEBA INFECTIONS.

Do organisms other than streptococci enter the human system through dental infections?

While the streptococcus seems universally to be present in dental infections in practically all cases of systemic involvement, in addition to this variety the evidence seems to establish that both staphylococci and spirochetes may pass from infected teeth to other tissues and proliferate in localized areas; and, similarly, that when certain mixed strains are injected into experimental animals, localized spirochete infections may develop in their tissues. Systemic involvements from spirochete infections and their localization in experimental animals are, however, relatively rare.

NO. 36. NUTRITION AND RESISTANCE TO INFECTION.

What is the relation of nutrition to resistance to dental infection?

The data at hand suggest:

(a) That the effects of variations in the diet do not express themselves quickly in specific defense.

(b) That variations in diet by the limitation of various vitamines produce effects which, in general, are similar to those of overload.

(c) Deficiency diets, particularly disturbances resulting in a calcium hunger, tend directly to lower the defense to dental infections.

NO. 37. THE RELATION OF THE GLANDS OF INTERNAL SECRETION TO DENTAL INFECTIONS AND DEVELOPMENTAL PROCESSES.

What is the relation of the glands of internal secretion to dental infections in developmental processes?

We would summarize these studies as follows:

(a) Disfunctions of various of the glands of internal secretion are often very materially corrected, and sometimes completely so, by the removal of dental focal infections.

(b) Involvements have frequently been produced in similar endocrine tissues of the animals by inoculating them with the cultures from the teeth of the involved patients.

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(c) The administration of the extracts of the glands of internal secretion, particularly of the parathyroid, is shown to be of distinct benefit in certain cases of depressed ionic calcium of the blood, due in part to dental focal infections, where this improvement has been absent or slow following the removal of the dental infections.

(d) An improvement has been produced in individuals, which we interpret to be due to a stimulation of the pituitary body, which in turn doubtless stimulates other ductless glands and together with them produces a marked change in both physical and mental states.

NO. 38. THE NATURE AND FUNCTION OF THE DENTAL GRANULOMA.

Is the dental granuloma a pus sac and its size a measure of the danger?

(a) The so-called granuloma is a misnomer, for it is a defensive membrane and not a neoplasm.

(b) A normally functioning periapical quarantine tissue is Nature's effective mechanism for protecting that individual by destroying the organisms and toxins immediately at their source, thereby completely preventing the tissues of that individual's body from exposure to either of these agencies.

NO. 39. CHANGES IN THE SUPPORTING STRUCTURES OF THE TEETH, DUE TO INFECTION AND IRRITATION PROCESSES.

What are the changes produced in the supporting structures of the teeth, which are due to infection and irritation processes?

Characteristic localized structural changes develop in the supporting structures of teeth when the latter carry infection within their structures. These changes are, however, determined chiefly by the host and are an expression of the reacting characteristics of the host rather than an expression of the invading bacterium.

NO. 40. DENTAL INVOLVEMENTS CAUSED BY ARTHRITIS.

Can arthritic infections of the body attack and devitalize the teeth?

(a) It will be seen from these data that a systemic involvement of multiple arthritis may, while attacking various joints of the

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body, also attack those of the joints of the teeth; and, further, that this process of inflammation with degenerative and proliferative processes may cause the involvement and ultimate death of the pulp.

(b) The involvement of these teeth as a result of the progressive systemic arthritis may in turn, and doubtless frequently, if not generally, does aggravate the general condition, for the tooth structure when it becomes infected is even less capable of vascularization and therefore less amenable to the processes of defense than is bone. This stresses the very great importance that individuals having deforming arthritis shall have most careful dental inspection and care, and also, since it is one of the most horrible of living deaths, every effort should be made to prevent the beginning of that process; and since the evidence is so overwhelming that the initial infection frequently, if not generally, comes from the teeth, helpless humanity deserves pity until the powers that be shall make a worthy effort to find the means that will prevent this needless catastrophe in so many lives.

NO. 41. VARIATIONS IN THE DEFENSIVE FACTORS OF THE BLOOD.

Is there a difference in the defensive factors of the blood of susceptible and non-susceptible individuals to systemic involvements from dental infections?

There is a marked difference, which is very readily measurable in the bactericidal properties of the bloods of individuals of high defense, as compared with those of low defense to systemic involvements from dental infections.

NO. 42. METHODS FOR REINFORCING A DEFICIENT DEFENSE.

Can a temporarily or permanently low defense against the streptococci of dental infections be increased or enhanced either temporarily or permanently?

In some individuals a low defense may be materially strengthened by the use of vaccines and also by the use of all available means for stimulating metabolism and increasing a supply of essential nutritional factors.

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NO. 43. SEROPHYTIC MICROÖRGANISMS.

What are the growth factors of microörganisms of the mouth in juices of living tissues?

When the mixed flora of the oral cavity are planted in the normal blood serum or lymph, the varieties that grow are almost entirely limited to the strains of diplo- and strepto-cocci, with occasional staphylococci, with the diplo- and strepto-cocci largely predominating.

NO. 44. CALCIUM AND ACID-ALKALI BALANCE.

What is the role of calcium in the maintenance of the acid-alkali balance of the blood, other body fluids, and tissues?

In the proper functioning of the body, the end products of metabolism are carbon dioxide, urea, and water. When metabolic functions are abnormal, resulting in the imperfect oxidation with the development of less simple acids than carbon dioxide, these must be neutralized with bases taken from the body and its fluids. In the absence of an adequate supply of these from other sources, the demand must be met by the calcium of the body, first from the circulating ionic calcium, then from the calcified tissues. This latter is the characteristic end reaction involved in periodontoclasia, or pyorrhea alveolaris. This enters into and complicates the etiology of many, if not most, of the rheumatic group disturbances studied in detail in subsequent chapters.

OLD INTERPRETATION

NO. 45. SYMPTOMS AND DANGER.

Since individuals are similar in their reactions to dental infections, both locally and systemically, and since freedom from involvements is dependable, the danger is proportional to the quantity and to the type or virulence of the dental infection involved and the patient's symptoms.

Since patients largely determine the biological qualities of the organisms involved in dental infections by the culture medium they furnish the bacteria, and since the sufficiently high defense of certain individuals will, under ordinary conditions, protect them from systemic injury resulting from their dental infections, and since the local oral expressions of the dental infection are an indication and a measure of that individual's reaction to the dental infection rather than a measure of that

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infection, therefore, it becomes apparent that the operation that is indicated is an individual factor and concerns the relation of the efficiency of the patient's defense to the attacking power of the dental infections and, accordingly, operations which are strongly indicated for some individuals are as strongly contraindicated for others.

NO. 46. DIAGNOSIS.

An adequate procedure for making dental diagnosis is a roentgenographic study of the patient, for which the only requisite training is a working knowledge of the apparatus and a familiarity with dental anatomy sufficient properly to call the teeth by their names.

An adequate procedure for making a dental diagnosis will involve, as a minimum, the following:

A knowledge of the patient's systemic defense and systemic involvements, both present and past. The securing of this will involve:

(a) A knowledge of the various systemic disturbances that may be produced or aggravated by the dental infection, with or without the patient's recognition of their existence. A knowledge of the systemic disturbances includes, for differentiating purposes, a knowledge of the etiological pathology of the involved tissues of most of the morbid conditions of the human body, regardless of the type of tissue or the involved nature of the functions. These are based upon a thorough knowledge of the gross and minute anatomy of the various organs and tissues of the body, and the normal functions of those tissues, with special reference to the nervous system.

(b) A roentgenographic study, with a knowledge that it is physically impossible for the Roentgen-rays to disclose much of the essential information, the roentgenogram being simply a record of relative total densities of the planes involved.

(c) A familiarity with the use of the microscope and such laboratory technique as serological study of the fluids of the body since many of the lesions, being produced or aggravated by dental infections, are in evidence by microscopic and chemical methods long before they appear clinically as symptoms.

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NO. 47. DIAGNOSTICIANS.

Dental diagnosis is so simple that any dentist or physician, osteopath, chiropractor, electrical engineer, or laboratory assistant, is competent to perform this simple service.

Dental diagnosis is so intricate and involved that it requires a greater knowledge of the human body, its structure and diseases, and of the various means for understanding the normality and abnormality of the same, than any specialty of the healing arts; and probably no specialty finds such great opportunity for doing injury to humanity, or for extending human life, as does the highest application of intelligence in this field. A competent diagnostician of the local and systemic expressions of dental infections must be familiar with the clinical and structural pathology required for a general medical diagnosis, and, in addition, be completely familiar with dental anatomy, dental pathology, and dental operative procedure.

This paragraph completes this presentation of researches on the fundamentals of oral and systemic expressions of dental infections. The practical application of these new interpretations is a continuation of the report of these researches and for convenience has been placed in a separate book as Volume Two, as Chapters 58 to 73. These will consider the role of dental infections in the development and progress of the degenerative diseases.

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