Some Systemic Expressions of Dental Infections[1]

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With the rapidly accumulating data relating dental infections to systemic involvements, particularly as contributing factors to the degenerative diseases, there is developing a distinct change in emphasis from the importance of the specificity of the organism to the importance of the specificity of the host. In the light of the newer knowledge, we are chiefly concerned with the soil. I have recently presented in much detail evidence tending to relate dental infections as important contributing factors to the degenerative diseases (1).

While the infection of periodontoclasia pockets, and of gingival lesions will consist of mixed infections, usually with spirochetes predominating, the locked infections of apical areas of tooth structure are practically always streptococcal with occasional incidental associated infection. The fact that streptococci are found in practically all dental lesions of the latter type is probably dependent upon the very remarkable range of adaptability of that organism to environment. With the reduction of oxygen tension, and the increase of CO_2 tension, the streptococci not only have the power of continued adaptability to changing environment, but with the change of environment, change their biological qualities in a way which apparently is distinctly to the disadvantage of the host. Rosenow has presented evidence indicating mutation changes between streptococci and pneumococci. Libman in a paper read before the Michigan State Medical Society, September 11, 1924, states:

> The aerobic streptococci are divided into hemolytic, nonhemolytic, or anhemolytic (so-called Streptococcus viridans) and the Streptococcus mucosus-capsulatus. The opinion which Dr. Cellar and I have had for many years that the anhemolytic streptococci represents transition forms between pneumococci and hemolytic streptococci is now receiving much support.

Libman's statement that the viridans group, anhemolytic streptococci represent transition forms between pneumococci and hemolytic streptococci is in complete accord with the earlier statement of Dr. Rosenow. I have undertaken to classify the strains of streptococci recovered from lesions in animals which had been inoculated with cultures from teeth of patients suffering from systemic involvement. In 100 successive patients so studied the strain of streptococcus isolated most frequently by this means was fecalis, which was found in 65 per cent of the cases. Next came infrequens 9 per cent; mitis 7.5 per cent; pyogenes 4.5 per cent; nonhemolyticus I, 3 per cent; nonhemolyticus III, 3 per cent; hemolyticus I, 3 per cent; ignavius, salivarius, and subacidus each 1.5 per

[1] Read before the American Congress on Internal Medicine, Detroit, Michigan, February 26, 1926.

cent. Of these, all produced a green zone on blood agar plates, hence were viridans, except hemolyticus I, subacidus, and pyogenes, which are hemolyzing strains. The strain of streptococcus most frequently found in the saliva is salivarius. It has ordinarily a very low disease producing quality. It is the strain which is most frequently available for the infection of caries and pyorrhea pockets. It does not, however, retain the sugar fermentation qualities which give it this classification, came finally to grow by suitable transfers in a concentration of 1:320. Similarly for a saturated solution of iodoform and alcohol, the organism changed from growing at the beginning in 1:80 to 1:10; with alcohol a change from 1:400 to 1:20; I have recently presented evidence (2) indicating a marked tendency to accommodation to various medicaments which are used for the treating of infected pulpless teeth. This probably explains why such a large percentage of extracted root-filled teeth

Effect of various medicaments on fermentation qualities during acquisition of tolerance of streptococci

MEDICAMENTS	1:100,000	1:50,000	1:37,000	1:25,000	1:18,000	1:10,000	1:6,000	1:1,250	1:800	1:600	1:500	1:400	1:300	1:250	1:200	1:180	1:160	1:140	1:120	1:100	1:80	1:60	1:50	1:40	1:30	1:20	1:15	1:10
Formalin						S.																						
Formocresol						S.		M.			M.																	
Mercurochrome						S.																						
Triolein						S.		M.																				
Lysol						S.		M.			F.																	
Oxpara						S.																						
Osogen liquid						S.		S.			F.			F.														
Natkalium						S.		M.			F.			F.														
Phenol						S.		S.			S.																	
Creosote						S.		M.			M.																	
Eucalyptol compound						S.		S.			M.			F.														
Chloroform						S.		M.			F.			F.						F.			F.					
Alcohol						S.		M.			F.			F.						F.			S					

Strain no. 43. Salivarius.

FIG. 1. MUTATION CHANGES IN STREPTOCOCCI IN THE PRESENCE OF IRRITATING MEDICAMENTS

All started as salivarius; nearly changed to mitis and then to fecalis with increasing concentrations of medicaments.

when growing under lowered oxygen tension, and increased CO_2 tension of devitalized bone or tooth structure.

The remarkable power of accommodation of organisms of the streptococcus group to various chemical compounds has been brought out in many of our studies. I have previously shown in Volume I, above referred to, that the strain of streptococci which required a dilution of formalin of 1:10,000 in order to permit of growth in the medium used. are found on culture to be infected, and greatly emphasizes the need for the development and utilization of means for the prevention of dental caries, rather than the present and past method of repair. The prevention aspect constitutes the chief emphasis of our research at this time. The influence of change of environment upon the biological qualities of the organisms is very important, which change may be toward the increase of virulence or disease producing quality, together

with the formation of a protecting capsule. This latter greatly reduces the ability of the host to react to a definite attack against the invading organism. The accumulating evidence strongly indicates that the irritation of medicaments may be a contributing factor in producing this unfavorable change in the quality of the organisms. These influences are shown in figure 1, which records the results when a number of disinfectants were added to culture media in various dilutions. A single strain is shown, no. 43, salivarius. In the creosote it changed to mitis; in triolein to mitis; in lysol, first to mitis then to fecalis; in osogen to fecalis; in natkalium first to mitis; then to fecalis; in phenol to fecalis; in eucalyptol compound first to mitis then to fecalis; in chloroform, first to mitis then to fecalis; and in alcohol first to mitis then to fecalis. In all of these medicaments, the change was in the direction of an increase in virulence. These data strongly suggest that we should expect an infected sequestrum, such as an infected tooth becomes, to be not only a source of grave danger as a zone in which organisms may thrive protected from the normal defenses of the body, but an ever-increasing danger because of the increase in offensive and disease-producing qualities. When there obtains a protected zone providing a lowered oxygen tension and increased CO_2 tension, a culture medium consisting of tissue degenerative products or with these depressing irritants, there is being developed a menace which in susceptible individuals may become an important contributing factor in the production of the degenerative diseases. This will probably occur through some of the means, and with some of the expressions presented in the following paragraphs.

ELECTIVE LOCALIZATION QUALITIES OF DENTAL INFECTIONS

While the enormous amount of evidence indicates elective localization of strains secured from dental infections for certain tissues of the body, I consider of far greater importance and significance the evidence that those qualities of the organism are an expression of the environment and culture medium furnished by the host. I do not mean by this that a child with endocarditis of necessity has the heart lesion before he has dental infection, but I do mean that the child with an inherited susceptibility to endocarditis furnishes a group of influences, one of which is provided in the sera of the body, which tend to develop a quality in the organism which makes it more readily attack that individual's heart. This might be illustrated in the following: A lad, fourteen years of age, was brought by the school nurse with a story that he had been suffering from rheumatism which had incapacitated him for a few days from school. The history of this case showed that he had one severe attack of toothache some six weeks previously. Following this an acute rheumatic pain developed which made it necessary for him to be helped home from school. The joint involvement subsided and he returned to school. The teacher sent a note to the parents that he was not interested in his play, and suggested that the visiting nurse see him. Our first examination revealed definite heart involvement. The tooth in question was found to have a vital pulp, though very deep caries. The pulp was not exposed. The tooth was removed under local anesthetic, and cultures made from the pulp tissue with great care to prevent contamination. Thirty rab-

bits were inoculated. Twenty-eight of the 30 developed carditis, and all of the 30 developed arthritis. The boy was taken by the visiting nurse to his home with instructions that he be kept in bed under the care of the district physician. The parents of the boy did not give proper co-operation with the to-be-expected result that the boy was buried in about six months. When this strain was grown for seventeen days under aerobic conditions in liquid medium and another group of animals inoculated, the virulence had been so greatly reduced that it now produced heart lesions in 10 per cent only of the animals as compared with 93 per cent when the fresh culture was used. The accumulating evidence seems strongly to suggest that chronic dental infections retained over a very long period of time can furnish means for reinoculation of susceptible hearts, and that one of the important factors which has compelled the conviction that heart leisons must always be considered very grave has been this factor of reinoculation but, as Libman and others have stressed, the emphasis is changing. Libman states (3):

> It is evident that I have presented the subject of the characterization of the various forms of endocarditis in a very broad way only. It is realized that the various subjects that have been discussed must later be taken up in a more detailed fashion. One thing is clear. It is evident that the disease which was considered rare, subacute bacterial endocarditis, is now recognized as one of the common diseases. Of great interest is the change in our point of view. It was supposed to be a practically uniformly fatal disease. Now we are observing more and more partial or complete recoveries. We find that very mild cases exist, and that there is a recurrent form of the disease. In other words, the interest is shifted toward the question of healing. It will be of the greatest value, if an active campaign is undertaken for the purpose of preventing this as well as other forms of endocarditis

If time permitted, we would desire to present many striking illustrations of elective localization. Typical of such would be shown in figure 2, in which will be seen the rotation of the rabbit's head from the culture taken from the tooth of a patient suffering from torticollis, and which was entirely relieved in the patient by the removal of the dental infection. When this animal was placed under an anesthetic, its head took a natural position only to return again when the animal came from the anaesthetic. Another and perhaps more striking illustration is that of a patient suffering from acute torticollis which prevented her from lying down for a week. It had been slowly developing with increasing severity during a period of two years, following the placing of a questionable type of dental restoration. (The denture was allowed to cover embedded roots.) The roots were removed with a very marked improvement in the neck involvement in twenty-four hours at which time a piece of the muscle of the neck was removed under aseptic conditions, part of which was cultured and another part sectioned. Figure 3 shows the streptococci within the sheath of a muscle fibre. Cultures were grown from the extracted roots and from the excised muscle tissue. Each culture was inoculated into a group of rabbits. Figure 4 shows two of these rabbits. "A" was inoculated with the culture from the tooth, and "B" was inoculated with the culture from the muscle. Both groups of rabbits had marked choreic movements, and displacement of the head as shown in the photographs. I have motion pictures of these two groups of rabbits showing very similar nervous and muscular system disturbances. In over two thousand rabbits which I have used in making these studies,

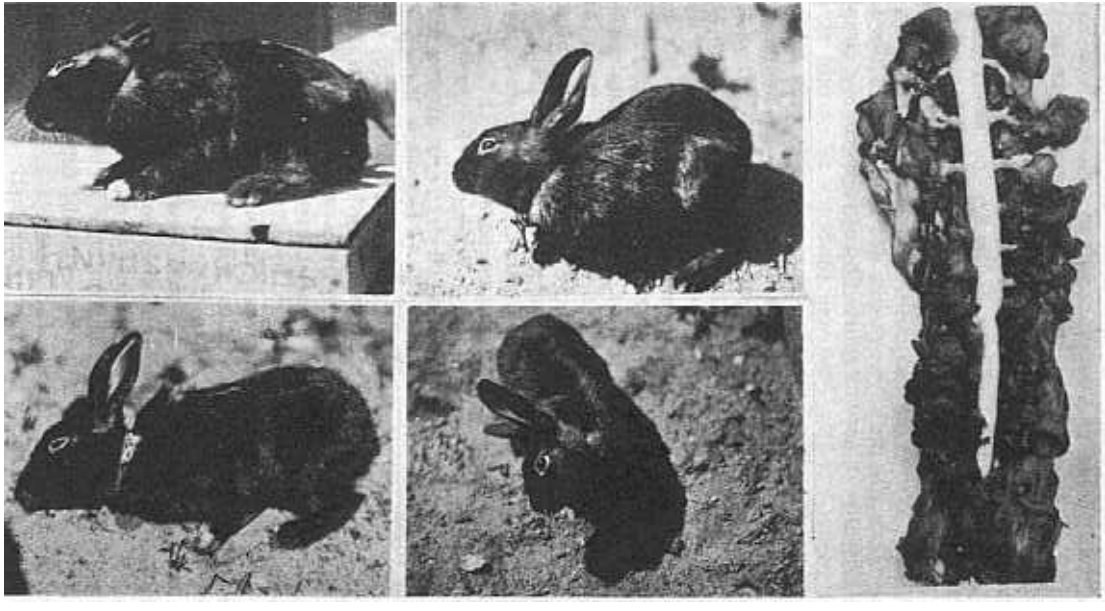


FIG. 2

This torticollis was produced with the culture from the tooth of a patient who had suffered severely for two years with recurring attacks of torticollis which attacks did not recur after the removal of the infected tooth.

similar lesions have not developed except with a few cultures and when they have developed, they have been characteristic of a large percentage of the group inoculated. This patient had no return of her torticollis for two years when it developed suddenly on the opposite side of her neck with the rotation of her head in the opposite direction. A tooth was found with an exposed pulp beneath a bridge. Within five hours after removal of the tooth the neck symptoms had practically disappeared and did not recur.

Another and very frequently seen

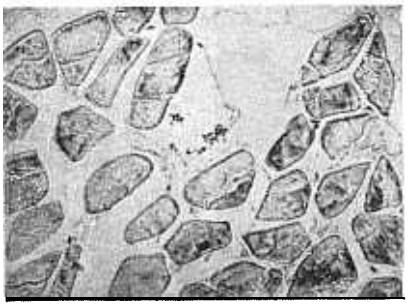


FIG. 3. STREPTOCOCCI WITHIN THE SHEATH OF A MUSCLE FIBRE

The tissue was removed from the neck of a patient suffering from torticollis which completely disappeared after the removal of dental infections. Part of the tissue was also cultured (see fig. 4).

illustration of localization is to be found in eye involvements. Figure 5, shows the eyes of rabbits with "B" normal, but "C" to "I" various stages of corneal ulcer terminating in complete blindness. Cultures were taken from teeth of the patient suffering from acute retinitis with approximately 1/5 vision as reported by the oculist who sent him. Five rabbits were inoculated with this culture, and 4 developed lesions in one or both eyes.

A striking illustration of involvement of the nervous system will be seen in figure 6, the roentgenogram of the teeth of a patient, a young woman, who is suffering from recurring attacks of an obscure nervous type. Four rabbits were inoculated with the culture from these teeth. Three of the 4 were paralyzed from the center of their spines backward.

Another important localization expression that has developed in our work has not so far as I know been reported by others, namely, the very marked tendency of certain strains taken from infected teeth to select ovaries and tubes. In figure 7, for example, will be seen an ovarian cyst which was as large as a small hen's egg, and which took about three months to develop. Six small ovarian cysts have developed in a single rabbit after inoculation with the culture from the tooth of a woman who had been operated on six weeks previously for removal of an ovarian cyst which was the size of a large goose egg. These are also shown in figure 7. In two thousand rabbits, divided approximately equally as to sex, such lesions have not developed in 2 per cent of female rabbits. In several cases, where the patient from whose teeth the culture was taken was suffering from ovarian involvement, a number of female rabbits have developed lesions. Direct smears and cultures made from the cyst shown in figure 7, showed Gram-positive diplococci which corresponded morphologically with those inoculated into the animal from the dental infection. I have previously reported a number of such cases.

Our usual method of inoculation has been to use about 1 cc. of an eighteen- to twenty-four-hour culture of a strain grown in deep ascites tubes containing dextrose

brain broth, usually with vaseline covering same. We have found that the elective localization qualities were very rapidly lost, particularly under aerobic conditions and that it is more important to have a young culture of organisms, even though scant in growth, than to have an older culture even though the latter is rich in growth. We have, for example, been able to produce acute endocarditis, which caused the death of the rabbit in two weeks, with the organisms washed from two infected teeth of a young man suffering from acute endocarditis. The calculated weight of the organisms injected as determined by a count for establishing the concentration was in the neighborhood of one millionth part of a gram.

I have done much work by placing infected teeth beneath the skin of animals through the smallest buttonhole incision that would permit of their entrance, care being taken not to contaminate the wound which was carefully closed with sutures and sealed. Approximately 75 per cent of such teeth caused the death of the animal in a few days or weeks and about 25 per cent became encapsulated which rabbits lived for months and frequently developed nephritis and streptococcal pneumonia sometimes after a year. One tooth was transferred from rabbit to rabbit to see if the virulence of the organism could be broken by this procedure. Thirty rabbits were

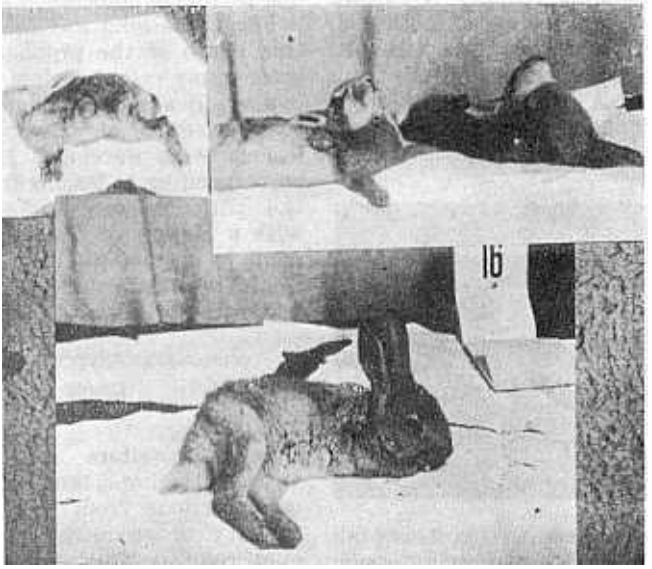


FIG. 4

These rabbits were inoculated with cultures from patients with torticollis. One of the two at the upper right with the culture from the extracted roots and the other with the culture from the neck muscle. Several rabbits from each group had neck involvement and choreic movements. The lower animal is paralyzed in his hinder extremities from the culture from the roots.

killed in succession, all but one in six days or less. This tooth had been removed from the mouth of a patient suffering from encephalitis. The chief symptom was recurring spasms of the muscles of mastication, chest, and arms. These repeated about every fifteen minutes and lasted for about five minutes. In the spasms, she would gnash her teeth so that it would be heard in the surrounding rooms. A culture was made from the above tooth and, inoculated subdurally into a rabbit, and at the same time a culture from a tooth of a patient not suffering from encephalitis was inoculated in a similar manner into another rab-

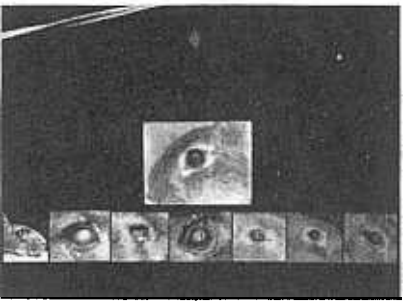


FIG. 5. EYE INVOLVEMENTS IN RABBIT INOCULATED WITH CULTURE FROM TOOTH OF PATIENT WITH ACUTE RETINITIS

The upper eye is normal. Of 5 rabbits inoculated with this strain, 4 had acute eye involvement.

bit. In a few hours time, the rabbit inoculated from the patient with encephalitis was having recurring spasms with gnashing of its teeth and spasms of the muscles of the forelegs and the muscles of mastication very similar to the expression in the patient. These two rabbits are shown, one in spasm, in figure 8.

In the light of the later work of Dr. Rosenow relating strains of diplococci to affections, simulating encephalitis, and in view of the results of our other inoculations with strains from patients not suffering from encephalitis, we feel impelled to give consideration to the association of these symptoms as produced in the rabbit with the infection from which the patient was suffering, quite regardless of whether the organism involved is a filter-passer or one of the streptococcus group.

For those who are interested in this phase of the problem I would refer to my recent review (4) which is made up almost completely of successive series of cases in which lesions were developed in animals corresponding to lesions from which the patients were suffering, and with a history of marked improvement in a large number of the patients with removal of dental infections.

SPIROCHETAL INFECTION OF THE LUNGS

Several writers have recently stressed the importance of spirochetal infections from the mouth as primary or secondary invaders in lung lesions. Kline and Berger (5) have reported 16 cases that have come to autopsy where the spirochetes were found in profuse numbers in the lung lesions. I have reported a case with the following history: A man about thirty-three years of age had a lung lesion which had been diagnosed as tuberculosis, was running a daily temperature, raising a very foul sputum, also had lassitude and was working only part time as a street car conductor. About his teeth were great quantities of spirochete infection, which organism is characteristic of periodontoclasia lesions. With the reduction of the gingival infection,

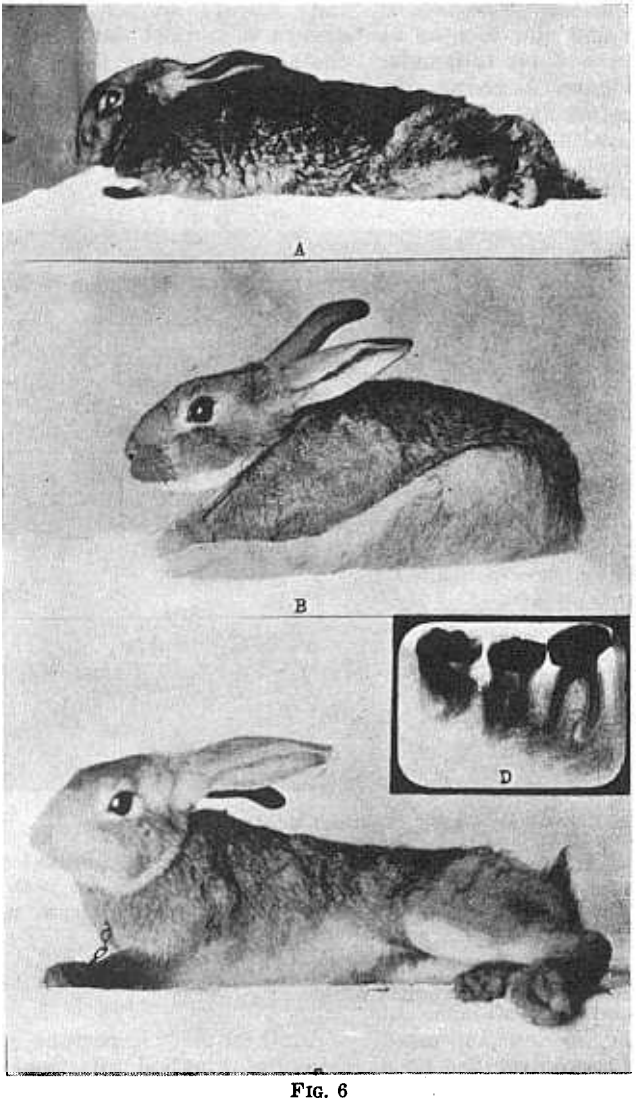


FIG. 6

These 3 rabbits are paralyzed from the center of their spines backward. Four were inoculated with the culture from the roots of the tooth shown, taken from a patient with severe but obscure nervous disturbance.

partly by extraction, and partly by treatment, he gained several pounds in a few weeks time, the afternoon temperature entirely disappeared and for a year and nine months he has had no return of his tubercular symptoms. Figure 9 shows the lung pictures before and six months after the removal of his dental infections. The diagnosis made by the lung specialist was for the first

marked tendency to periodontoclasia, or pyorrhea alveolaris, and since pyorrhea infections are practically always spirochetal, there is always a marked danger of spirochetal involvement from pyorrhea pockets as a complication with tuberculous infection. The spirochete would usually be difficult to recognize except as the result of special search.

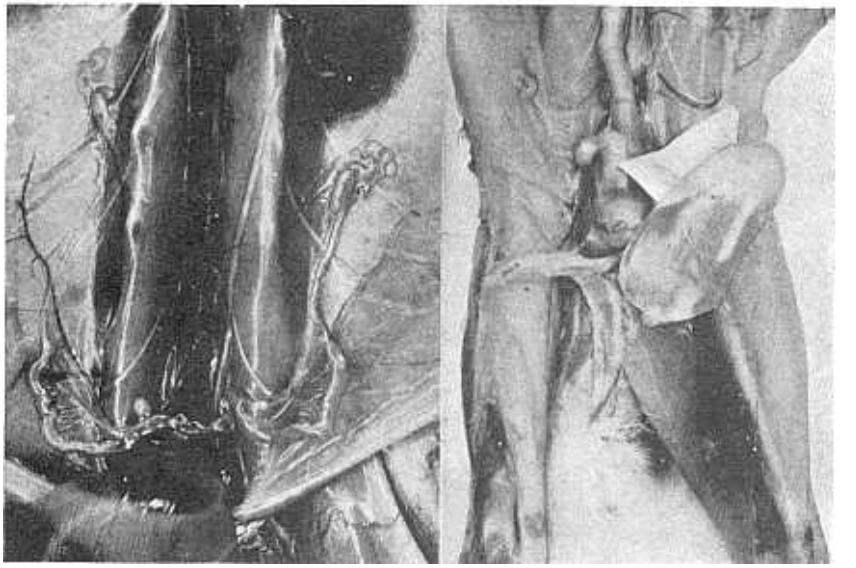


FIG. 7. OVARIAN CYSTS PRODUCED BY DENTAL CULTURES

The one to the right was as large as a small hen's egg. The rabbit at the left had six ovarian cysts. It had been inoculated with the culture from the tooth of a woman from whom had been removed an ovarian cyst as large as a goose egg six weeks previously.

study probable tuberculosis, and with the second, no evidence of tuberculosis and he now expressed the doubt that there ever had been a tubercular infection. Since the type of patient who makes the poor fight against tuberculosis is of a decalcifying type, and since the decalcifying type patient has a

HEMOPHILIA

Another very important complication of gingival infection which should be emphasized will be found in those types of organisms which produce primary and secondary anemia. Some strains of streptococci show marked tendency to

hemolyze red blood cells. We see these cases frequently presenting with disturbances of clotting and death is not infrequent from slow spontaneous hemorrhage from the gums. Such a severe case is the following: A young man, about thirty years of age, suffered from hemorrhage from his gums for a period of three months, practically continuously night and day. On two occasions, he became unconscious from loss of blood and was given transfusions. A hemorrhage into the internal ear had produced complete deafness in that ear. His clotting time was about ten minutes. Close examinations showed that the hemorrhage was greatest about his pulpless teeth. Cultures from one of these teeth inoculated into rabbits produced multiple spontaneous hemorrhage throughout the body. Figure 10 shows the hemorrhages in the thigh and kidney of a rabbit which died in twenty hours after inoculation with this strain. The rabbit practically bled to death from hemorrhage into its tissues. With the removal of this patient's infections, and the use of a vaccine made from these strains, his clotting time was rapidly reduced to three minutes and in five weeks time he was back on the road as a commercial traveller. I have reported similar strains that have killed animals in eight hours by multiple spontaneous hemorrhages.

PRIMARY AND SECONDARY ANEMIA

A new interest in the gingival infections is to be found in the recently reported studies on the relation of the yeast Monilia psilosis, and its effect in sprue and anemia. Ashford (6), working in Porto Rico, reports finding this yeast organism to be present in a very large percentage of the cases of sprue which is very prevalent there. Grove, Vines, Shelton and others, not only found the blood calcium lowered in sprue but have been successful in treating that affection by the use of para-

FIG. 8. INTRADURAL INJECTION OF CULTURE FROM TOOTH OF A PATIENT WITH ENCEPHALITIS

The rabbit to the right has spasms of the muscles of mastication and forelegs, very similar to those suffered by the patient. The rabbit to the left was similarly injected with culture from tooth of a patient not suffering from encephalitis. It did not develop similar symptoms.

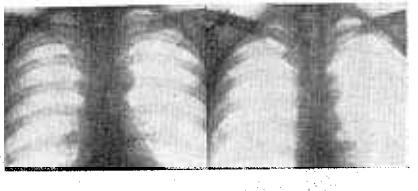


FIG. 9. IMPROVEMENT IN LUNG CONDITION BY REMOVAL OF SEVERE PYORRHETIC TEETH FROM A PATIENT WITH TUBERCULAR SYMPTOMS BUT WITHOUT TUBERCLE BACILLI IN THE SPUTUM

thyroid and calcium lactate. Wood (7) has stressed the probable relationship between sprue and pernicious anemia, since he has found the Monilia psilosis in gingival infections and feces in large numbers in both groups. We have not been able to find this organism in the

mouths of normal individuals in Cleveland.

Strains of Monilia psilosis, obtained from pyorrhea pockets and from feces of patients suffering from pernicious anemia and sprue have been run in rabbits divided into three groups. Group "A" has received cultures of the organism by stomach tube directly into the stomach. Group "B" has received the exotoxin as a bacteria-free ultrafiltrate, obtained by use of a celloidin sack and 150 mm. mercury pressure. Group "C" received an endotoxin secured by separating the organisms by centrifuging and washing in several changes of nor-

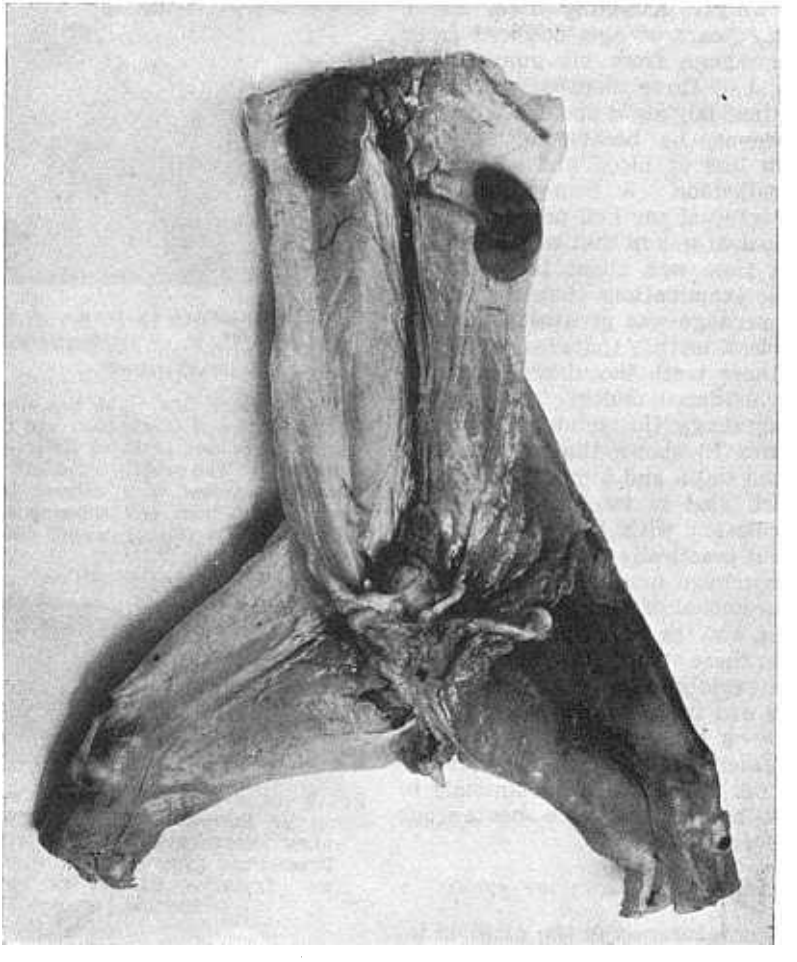


FIG. 10. MULTIPLE SPONTANEOUS HEMORRHAGES IN RABBIT CAUSING DEATH IN TWENTY HOURS FROM CULTURES FROM TOOTH OF PATIENT, PROSTRATED FROM SPONTANEOUS HEMORRHAGE FROM THE GUMS

mal salt solution. The organisms were then ground with sand in a tumbler for several hours and the material separated. One of the characteristic reactions in group "A" (which group received the organisms by stomach tube) has been an increase in a weeks time of total calcium of the blood of 20 to 30 per cent, without a corresponding increase in inorganic phosphorus. The diffusible calcium has increased to about the same extent. Some strains have proven to be much more toxic than others as several of the rabbits have died within a few days after beginning the treatment. There is, however, a marked difference in the virulence of the different strains. Polychromatophilia, anisocytosis, and poikilocytosis have been found in a number of these rabbits, as have also nucleated red cells. The rabbits of group "B" receiving the exotoxin injected directly intravenously have most of them died within a few days time, especially with the exotoxin from certain of these strains. Most of them have died before extreme blood changes have developed, though several have developed quite striking changes such as reduction of erythrocytes, increase of color index, nucleated reds, polychromatophilia, anisocytosis and poikilocytosis. The toxicity of the endotoxin used in group "C" has been markedly less than that of the exotoxin. Some changes in blood morphology have developed in this group, and an important characteristic has appeared in the blood chemical studies as a reduction in total calcium. In one of these rabbits about 30 per cent of the red cells contained bodies resembling the malaria plasmodium. Figure 11 shows two specimens of blood, one taken from a patient with pernicious anemia in an advanced stage, and the other from a rabbit which received the bacterial product of the culture taken from the pyorrhea pockets of a pernicious anemia patient. The patient's case of several years standing, has been developing for about as many months as the rabbit's has days. They cannot, therefore, be considered comparable in history. It is of importance, however, that many points of similarity are evident. This patient with a venous erythrocyte count of 1,439,000, and 29 nucleated red cells in counting 235 leucocytes, has a total calcium of 8.9, diffusible calcium of 5.4, non-diffusible or colloidal of 3.3, which constitutes so serious a hypocalcemia as to greatly disturb all organ and tissue function of the body. Other characteristics of this patient's blood were marked polychromatophilia, poikilocytosis and anisocytosis. His hemoglobin was 30 (by Dare), leucocytes 5800, Arneth index 52, polymorphonuclears 44.7, small lymphocytes 52.3, large lymphocytes 2.9, transitionals 2.9, basophilic cells 1.2, with no eosinophils. I will presently present data indicating that one of the body's early reactions in the presence of infections which disturb calcium levels is to increase the total calcium as a means of holding up certain depressing calcium factors. The accumulating data bearing on the relation of monilia psilosis to pernicious anemia, strongly suggest that calcium disturbances are not only one of the important changes involved but that they directly contribute to several of the blood changes such as the production of leukopenia. Owing to the extreme toxicity of the bacteria-free exotoxin, it has been necessary to reduce the quantity of intravenous injection, since many of the rabbits died within a few days with characteristic central nervous system disturbances which drew the

head backward and those that were observed while dying suffered violent clonic contractions with indications of marked disturbances in

ported a series of pernicious anemia cases in which the major symptoms appeared as brain and cord lesions and they have stressed the import-

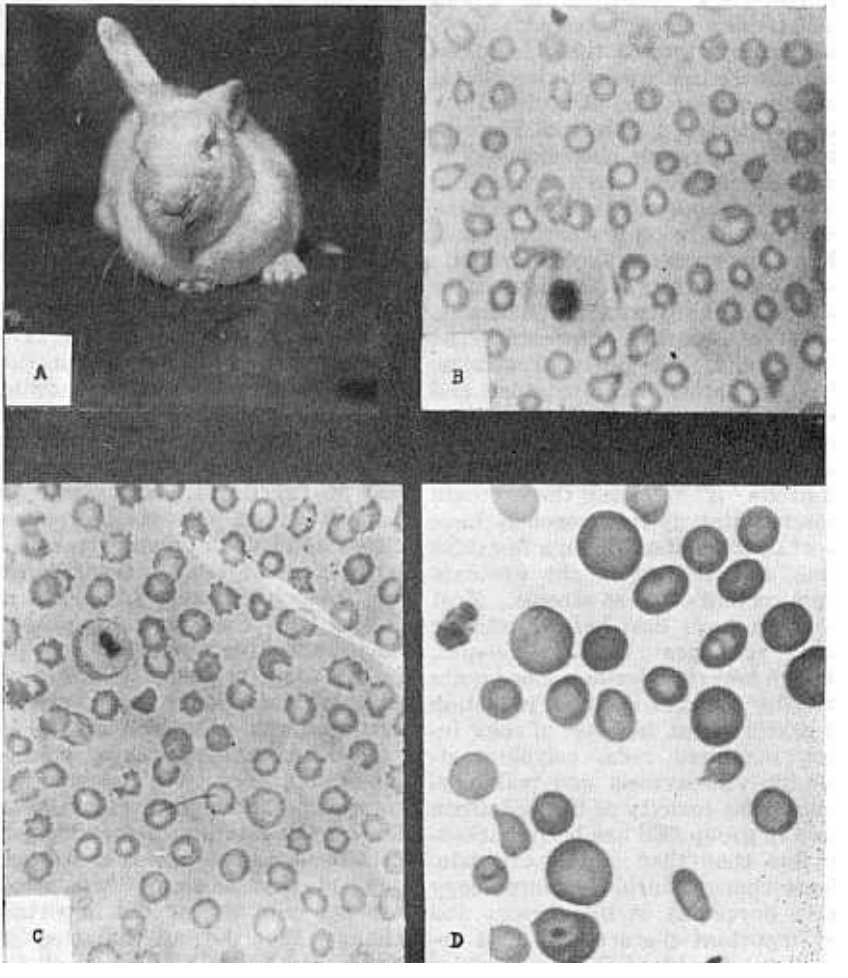


FIG. 11. ANEMIA AND SPRUE STUDIES

Cultures taken from pyorrhea pockets of patients suffering from same. *A*, a paralysis of side of the face, and part of side from placing culture in stomach by stomach tube. *B* and *C*, blood cell changes produced in rabbits. *D*, blood smear from patient with anemia.

brain and cord. These tissues are being run for pathological changes. Reese and Beigler (8) recently re-

ance of lesions of the nervous system as being usual involvements. Whether it shall be demonstrated

that pyorrhea infections constitute an important etiological factor in pernicious anemia, the evidence compels very serious consideration, and necessitates a program of exacting treatment and prevention, if pyorrhea is not to be a common contributing factor in the various primary and secondary anemias.

COMPLEMENT FIXATION

In our complement fixation studies data have been secured strongly indicating that strains of organisms cultured from infected teeth tend to show a positive complement for the blood of the individual from whose mouth the teeth were taken. We have used a number of our own stock antigens and a number secured from Dr. Burbank of New York. For example, patient no. 1650 presented a mild anemia. Her blood was tested with ten antigens one of which was made from her own tooth, to which she had a four plus reaction. The strain was viridans. She was positive to three of our standard strains all of which were hemolyzing strains. Also another patient who had been bedridden much of the time for the past year with arthritis of the spine was positive to seven strains of which five were from arthritis deformans cases, one from periarticular arthritis and one from perisynovial effusion. A number of patients were positive to antigens from arthritic cases who had had mild attacks of arthritis but who were not suffering from same at the time of the test. One patient who was completely rigid in his right knee and hip and almost completely so in the spine was positive to only one standard antigen. It was a Streptococcus hemolyticus from an arthritis deformans case. Two strains of streptococci recovered from his urine, one a mitis, and the other an ignavius, and which were not killed by his blood, when incubated with it for twenty-four hours, were used for making antigens. These antigens, when tested with his blood were both strongly positive. When his blood was vaccinated in vitro with a vaccine made from these strains there was a change in the bactericidal efficiency from 5000, 10,000, and 15,000 colonies per unit area to 0 in twenty-one tests, and 1, 19 and 56 colonies in three other tests. In other words, more than 99 per cent of all the organisms in twenty-four tests were destroyed by the vaccinated blood in vitro. These illustrate our method of selecting the strain from which to make a vaccine and the checking of the vaccine before using it on the patient. The difference between the 5000, 10,000 and 15,000 was caused by the difference in the time the organisms were in contact with the vaccinated blood. When in direct contact for four and one-half hours, 15,000 colonies grew out; twenty and one-half hours, 10,400 colonies; and forty-four hours, 5,200 colonies.

MORPHOLOGICAL AND CHEMICAL CHANGES IN THE BLOOD

The rapidly accumulating data regarding blood stream changes and their significance suggests strongly to the writer that the changes in the cellular and chemical constituents of the blood present an argument for the elimination of chronic dental infection which is even more important than the clinical data. Chronic dental infections tend to produce a change in the leucocytes as a relative depression of the polymorphonuclears and an increase of the small lymphocytes. This is the condition which presents when infected teeth are placed beneath the skins of rabbits. During the period of ac-

tive aggressive warfare, there is an increase in the polymorphonuclears, which soon changes if the animal is to be overcome by the presence of the tooth as occurs in 75 per cent of the animals in a few days or weeks. This is typically illustrated in figure 12, which shows the progressive changes. The polymorphonuclears decrease from 57 to 31 per cent, and the small lymphocytes increase from 34 to 62 per cent. A group of patients with chronic dental infections are shown in figure 13, in which it will be seen that in all of the cases presented the polymorphnonuclears were below 55 per cent and the small lymphocytes usually above 35 per cent. This phase has been conspicuous for years, and our studies have been concentrated quite intensively upon the causative factors. By returning to figure 13, it will be noted that the active calcium at first increased as did also the total calcium but that the active soon decreased while the total was still increasing. This seems to be part of the natural mechanism for holding up certain calcium factors which are being depressed. On the fourth day, the active calcium was at 9.4 or more than 2 mgm. below the starting point, while the total was 0.6 mgm. above its starting point. We have made these observations many hundreds of times and have found continually that as the rabbits' active calcium has become depressed to about 5 or 6 mgm., the rabbits go into convulsions and die. This will often occur with the stomach full of freshly taken food. This has led us to intensively study the various calcium factors in relation to chronic infections, dental and otherwise.

Any observations as to comparative levels will of necessity be on the presumption that relative normals are known. The literature on the question of various calcium levels furnishes much data regarding the total calcium but very little regarding other factors. Even normal total calcium is given quite wide latitude. My own studies have indicated that there is a difference in what constitutes the normal level for different individuals, and further that individuals can be divided into three groups on the basis of the presence or absence of susceptibility to rheumatic group affections, and also on the basis of the type of reaction in bone in the presence of dental infection, which groups will

Comparison of changes in blood morphology and calcium due to culture inoculations

DATE 1923	HEMOGLOBIN	ERYTHROCYTES	LEUCOCYTES	POLYMORPHONUCLEARS	LYMPHOCYTES		BASOPHILES	ARNETH INDEX	CALCIUM ACTIVE	CALCIUM TOTAL
					LARGE	SMALL				
6–1*	85	6,900,000	15,000	57	7	34.	2	83	11.53	13.00
6–2	85	6,150,000	27,700	70.1	14.4	15.4		48	11.80	13.22
6–4	80	5,750,000	19,800	35.5	8.8	53.3	2.4		9.45	13.66
6–5	80	5,800,000	16,600	64.7	16.8	17.9			8.46	8.71
6–6	85	5,100,000	14,800	31.2	6.4	62.4			8.05	9.80

* Before inoculation. (Case No. 1406. Rabbit No. 1221.)

FIG. 12. SHOWING MARKED REDUCTION IN POLYMORPHONUCLEARS, AND INCREASE IN SMALL LYMPHOCYTES ASSOCIATED WITH DECREASE IN TOTAL AND ACTIVE CALCIUM PRODUCED BY THE INJECTION INTO THE ANIMAL OF STREPTOCOCCAL CULTURE

show a difference for what may be considered normal calcium levels. Further my researches show that we will have the same individuals in the various groups by each of systemic defense and susceptibility. Typical illustrations of the difference in dental pathology in these different groups are shown in figure 14. "A" and "B" show very large

Blood morphology of clinical cases showing typical low polymorphonuclears and high lymphocytes

CHART NUMBER	HEMOGLOBIN	CELL VOLUME	ERYTHROCYTES	LEUCOCYTES	COLOR INDEX	WALKERS INDEX	ARNETH INDEX	POLYMORPHO-NUCLEARS	SMALL LYMPHOCYTES	LARGE LYMPHOCYTES	MONONUCLEARS	BASOPHILS	EOSINOPHILS
	per cent	*per cent*						*per cent*	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*
1237	98	44.5	5,680,000	6,200	0.96	−0.2	75	45.1	42.2	5.8	3.3	0.5	1.1
1233	100	33.4	4,860,000	7,000	1.04	−0.9	68	42.2	40.0	9.2	4.5	1.3	2.8
1213	98	43.0	5,672,000	5,400	0.95	−2.0	57	52.2	42.1	2.1	1.4	2.2	
1198	97	53.0	5,080,000	5,400	0.97	−1.0	53	45.4	45.2	4.4	0.7	0.7	3.6
1197	100	51.0	5,830,000	4,800	0.86	−2.4	61	50.7	32.2	4.3	1.4	0.7	10.7
1189	95	49.2	5,190,000	6,200	0.90	−0.4	58	46.5	47.0	2.4	2.9	0.6	0.6
1187	97	44.5	3,620,000	4,270	1.32	−2.8	53	50.0	42.0	3.5	1.1	0.5	2.5
1186	94	49.5	6,060,000	7,400	0.78	−0.1	58	52.9	39.8	4.0	1.8	0.5	1.0
1183	105	50.5	4,840,000	4,600	1.10	−1.8	72	44.8	44.8	5.4	2.5	0.4	2.2
1182	97	42.0	4,780,000	5,300		−1.8	68	51.2	41.4	4.1	1.2	1.2	1.2
1179	98	43.5	5,560,000	5,400	.087	−1.7	63	50.0	40.0	6.5	2.0	0.0	1.5
1175	92	46.0	5,060,000	8,600	0.89	−1.3	70	51.0	35.1	6.4	3.7	0.6	3.2
1173	98	50.4	6,100,000	8,000	0.81	−1.4	68	53.0	41.0	1.2	1.2	0.6	3.0
1171	100	49.0	5,060,000	8,400	1.00	−1.2	70	50.0	38.0	1.6	1.6	1.1	2.7
1168	98	39.5	6,200,000	10,000	0.80	−3.1	61	48.3	45.4	2.8	1.7	0.6	1.2
1164	90	50.5	4,840,000	4,400	0.94	−2.6	67	48.6	33.3	9.8	3.8	0.0	4.5
1163	95	46.0	5,575,000	5,400	0.86	−1.1	69	45.5	38.5	4.0	4.5	6.0	1.0
1149	96		6,600,000	19,200	0.87			40.2	14.5	6.0		0.0	38.5
1146	98		5,450,000	4,200	0.91	−3.4	71	53.2	33.4	5.7	2.8	1.4	3.5
1143	85		4,930,000	5,000	0.86	−3.7	64	52.6	35.5	5.9	1.8	0.6	3.6
1133	80		4,520,000	9,000	0.89	−1.9	67	50.0	41.4	2.6	1.6	1.1	3.3
1131	85		5,100,000	7,300	0.84	−0.0	66	48.0	39.3	5.4	3.8	0.0	0.5
1130	90		5,675,000	7,000	0.85	−0.2	55	50.0	39.0	4.0	5.0	2.9	1.1
1123	85		5,650,000	7,600	0.80	−0.5	71	53.0	37.5	5.0	2.5	3.5	0.5
1121	80		5,920,000	5,200	0.76	−2.3	57	51.0	41.8	1.2	1.6	1.2	1.2
1114	85		5,344,000	5,400	0.83	−1.9	58	52.5	35.6	6.0	5.5	2.0	0.5
1112	85		5,640,000	7,800	0.80	−0.3	60	50.0	37.0	4.2	4.2	1.6	0.5
1110	85		4,680,000	6,400	0.85	−0.7	44	52.1	40.0	4.0	2.5	0.5	3.0

FIG. 13. A GROUP OF PATIENTS WITH CHRONIC DENTAL INFECTIONS, SHOWING CHARACTERISTIC DEPRESSION OF POLYMORPHONUCLEARS AND INCREASE IN SMALL LYMPHOCYTES

these two methods of classification. There is, therefore, evidence of a direct relationship between the type of reaction in bone and the type of areas of rarefaction about the apices of roots with putrescent pulps. These individuals have a history of complete freedom from rheumatic group

affections, and their large zones of rarefaction are direct evidence of good capacity for making a local reaction which constitutes a quarantine between the infected tooth and the host. On the basis of dental pathology, I have classed the individuals of this group as the decalcifying type, and on the basis of their history of the rheumatic group lesions, I have classed them as the group with the *absent susceptibility*. "C" and "D" represent the next group, characterized on the basis of dental pathology, with a zone of more or less extensive condensing osteitis about a zone of rarefaction. These are the individuals whose type of local reaction has changed. Incidentally the quarantine is not efficient and the organisms and toxin from the infected teeth are not destroyed and can invade the patient. On the basis of clinical history or disease susceptibility, we class them as the group with the *acquired susceptibility*. These individuals are physically breaking, and the process may or may not have gone to the point where the patient complains of definite symptoms or localized lesions. "E" and "F" are characteristic of the individuals of the third group who on a basis of dental pathology have very little evidence of reaction about teeth with putrescent pulps. There is marked absence of adequate reaction about the root apex, and the toxic material and infection can invade the patient. The teeth are not sore, are difficult to extract and constitute at once the type with greatest danger and the greatest probability of being entirely overlooked or passed on the basis of insufficient evidence of pathology. On the basis of clinical history, these individuals tend to have recurring attacks or some rheumatic group affection or affections. Whereas in the two former groups, the other members of the family have been largely free from rheumatic group disturbances, in this group, on the contrary, there is a marked inherited susceptibility. We accordingly term them the individuals with an *inherited susceptibility*.

I have presented data in several communications (9) indicating that the calcium levels tend to be different in these different groups, and if time permits, I shall desire to present evidence indicating that defense and susceptibility are directly related to calcium levels, and to factors of calcium metabolism. In order further to make clear the difference in these three groups, I present in figure 15, resistance and susceptibility chart together with typical roentgenograms of a patient that would be in the first of the three groups by each of the two methods. On the basis of dental pathology, it will be noted that there is a very marked decalcification about the involved teeth. There is evidence, therefore, of a splendid defensive mechanism which maintained a quarantine between the infected teeth and the host. Note in the first two columns the patient's history showing quite complete absence of rheumatic group affections with only an eye involvement to seriously disturb. The patient has seven brothers and three sisters, all of whom have been free from rheumatic group affections. Both sides of the ancestry, including the father and mother, the four grandparents, and the uncles and aunts on both sides are shown to be free from rheumatic group affections. You will later see that the calcium in this group tends to be high. Figure 16 shows the zone of calcification about a zone of rarefaction. This girl, at twenty-two, has had influenza: she has had two serious

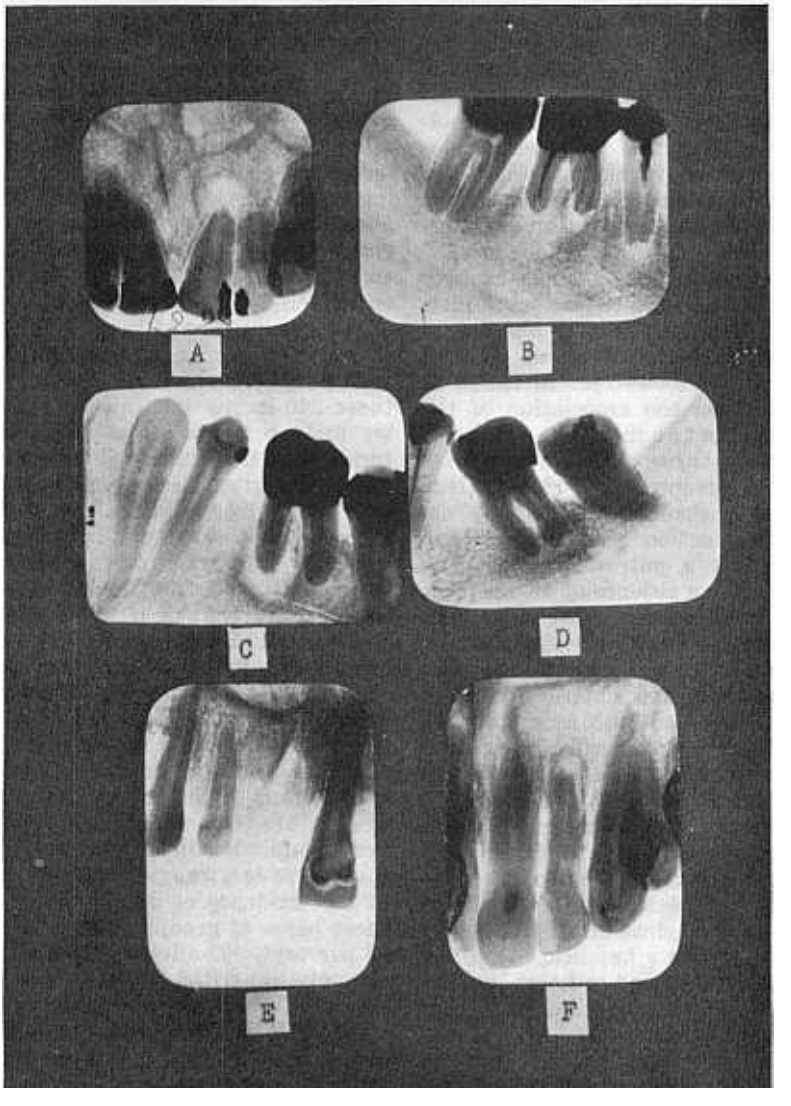


FIG. 14. CLASSIFICATION OF INDIVIDUALS INTO THREE GROUPS ON THE BASIS OF THE TYPE OF REACTION IN BONE ABOUT INFECTED TEETH

A, and *B*, marked decalcification and cavitation with root resorption. *C* and *D*, condensing osteitis surrounding rarefying. *E* and *F*, relatively little reaction compared with quantity of infection.

dental infections, has a nervous breakdown following influenza and does not recover. With the removal of the dental infections she makes a very rapid improvement. On the basis of the dental pathology, we have the condensing osteitis, about the rarefying. With her broken defense from influenza she ceases to maintain the quarantine. From the resistance and susceptibility standpoint she would classify as having an acquired susceptibility. Note the quite complete absence of rheumatic group affections on both sides of the ancestry. In figure 17 will be seen the association of the data by the two methods. This girl at twenty-three, is an invalid with heart involvement and rheumatism. Note the absence of adequate defensive reaction about the lateral which has a putrescent pulp, and therefore, an absence of an adequate local quarantine. Note that this girl, who is breaking with heart involvement, and rheumatism has five brothers and sisters, several of whom have had both heart involvement and rheumatism. Her father and mother are both dead at about fifty years of age with heart involvement. There are eight cases of rheumatism in the family and nine of heart involvement, four of whom were dead at the time, and another has since died. This girl was born with a handicap. She not only is predisposed to heart involvement and rheumatism, but very strongly predisposed to dental caries, and therefore, to pulp involvement with its inevitable periapical infection.

If we arrange these individuals on the basis of these various groupings, *absent, acquired,* and *inherited susceptibility,* and divide the inherited group into four subdivisions—one side mild, two sides mild, one side strong, two sides strong—referring to the strength of the inheritance, it will be noted that there is a marked difference in the incidence of rheumatic group affections, in the individuals of these various groups. I have now made susceptibility records for over 1600 individuals and their families and in making my deductions, I have not used about half of these because of incompleteness in some parts of the record. In this chart, I have selected fifteen typical families for each of the groupings and in each family there would be on an average, fifteen people recorded for study. In these 240 individuals in each group, we find on the basis of their histories that the records show severe rheumatic group lesions, in the absent group 16, acquired group 63, inherited one side mild 144, inherited two sides mild 227, inherited one side strong 258, inherited two sides strong 483; or if we take the severe and mild rheumatic group lesions, the figures are respectively 31, 96, 201, 308, 338, 754. The individuals, therefore, who are born in the last group are more than 20 times as much in danger of rheumatic group affections on the average as are the individuals in the first group. It will further be noted that there is a progressive increase in the incidence of dental caries on these bases of groupings from 40 to 93 per cent. The individuals in the strongly inherited group show an incidence of 93 per cent with dental caries. It is of interest that the group with the *acquired susceptibility* namely, those who have recently broken from overloads, show an incidence of caries twice that of the individuals in the *absent* group. On the basis of presence or absence of pyorrhea alveolaris it is of great significance that this affection decreases in incidence as we descend this order of grouping. You are

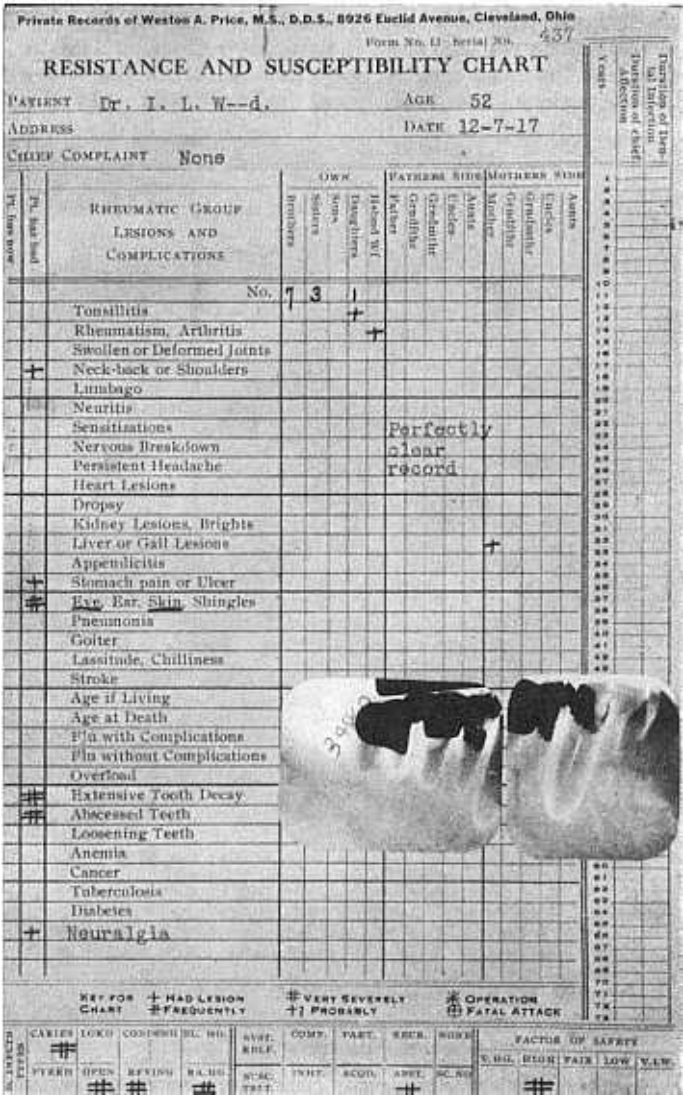


FIG. 15. ABSENT SUSCEPTIBILITY GROUP

Note the clear record of patient and family from rheumatic group affections and marked decalcification and rarefaction about infected teeth.

doubtless all familiar with the clinical fact that caries is practically never found in pyorrhea pockets. However, since both pyorrhea lesions and caries lesions persist, the two may develop in the same mouth at two different periods, and both

viduals with a high defense for rheumatic group affections. If time permitted I could furnish abundant evidence indicating that in most individuals periodontoclasia or pyorrhea is a defensive reaction against local irritants and that there are

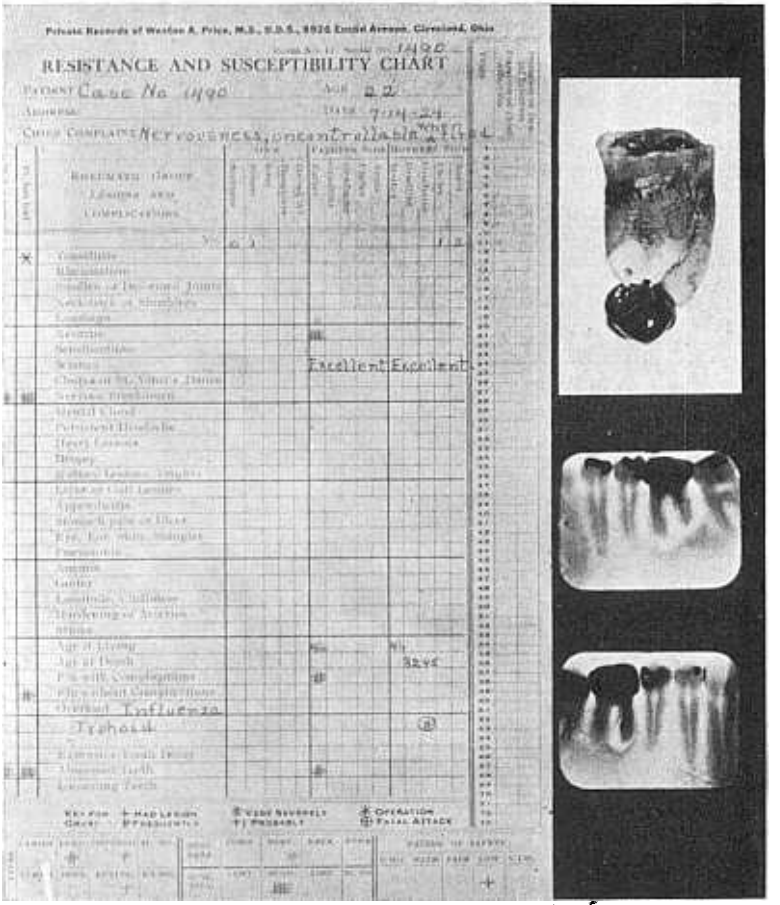


FIG. 16. ACQUIRED SUSCEPTIBILITY GROUP

Nervous breakdown following influenza. Note condensing osteitis surrounding rarefying and absence of rheumatic group affections in family.

be recorded in the skeleton. Note that the individuals with the marked tendency to periodontoclasia or pyorrhea tend to be the indi-

several systemic factors one of the most important of which is good capacity for a defensive reaction. These individuals tend, while hav-

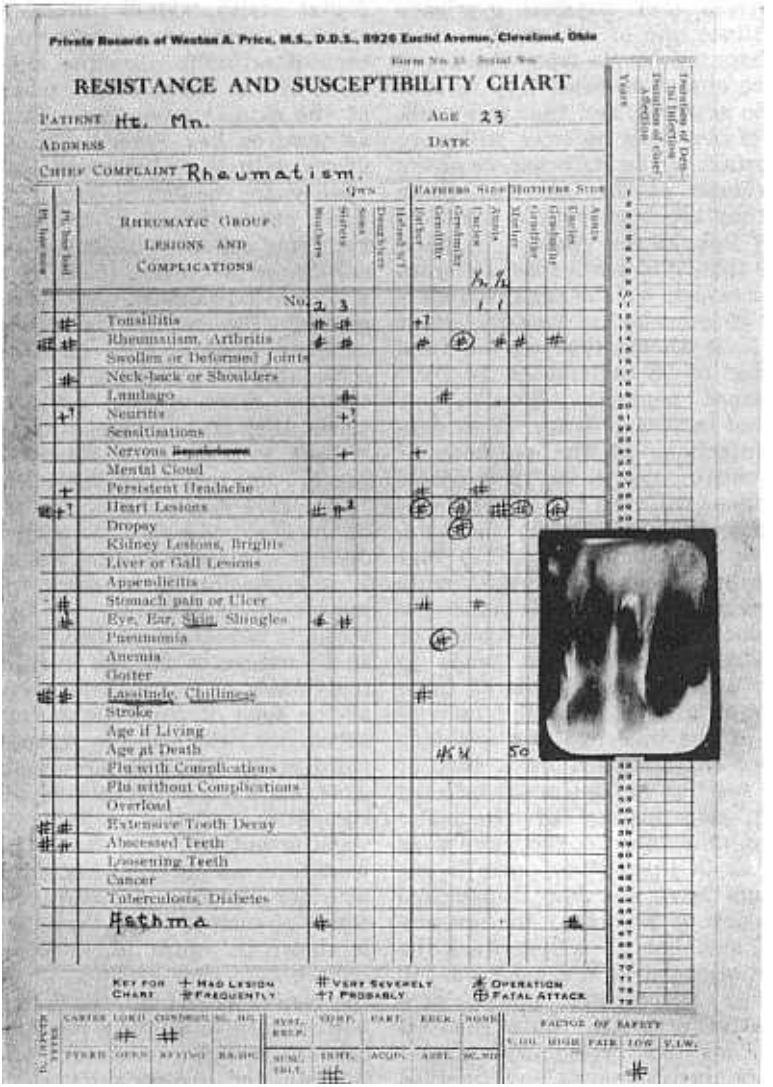


FIG. 17. INHERITED SUSCEPTIBILITY GROUP

Note many rheumatic group disturbances in patient and family, particularly heart and rheumatism and absence of adequate apical reaction.

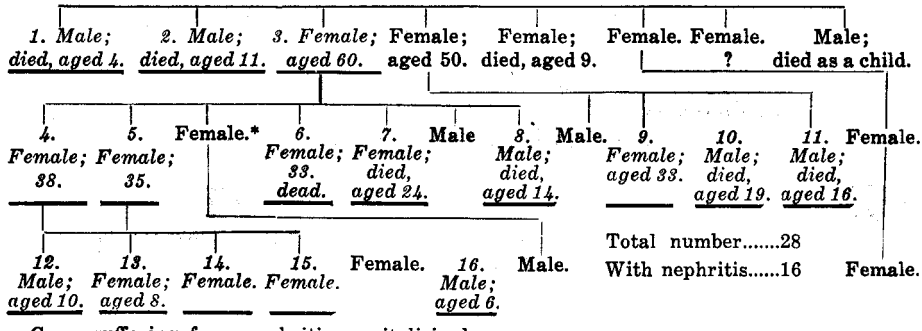
ing this high defense, to have high calcium levels. In passing, I wish to stress that physical overloads constitute one of the chief factors in changing people from the group of the absent susceptibility to that of the acquired, and that this problem of overloads becomes still more important in the disturbances of the individuals of the inherited group for they are born with a definitely weak link in the chain. To illustrate this point I will refer to figure 18, in which will be seen reproduction of genealogical tree by Hurst (10). It shows that in the total number of 28 individuals, 16 have developed nephritis. Hence their marked increased danger from dental infections in the presence of systemic overloads, for their dental infections will tend to express themselves in this weak link in the chain. I have previously shown (11) that there is evidence of a relationship between the type of systemic disturbance, whether streptococcal or non-streptococcal, which tends to develop in the individuals of these different groups, that the individuals of the inherited susceptibility group, characterized by a lack of local reaction in bone about infected teeth, and history of rheumatic group affections in the family as well as in themselves, have a low calcium level and low bactericidal efficiency of the blood for streptococci, and that when they break the affections tend to be among the following: heart involvement, proliferative arthritis, acute rheumatism, nervous breakdown, stroke, kidney involvement, and marked tendency to dental caries. The group with the acquired susceptibility, characterized by condensing osteitis about rarefying osteitis, tends to have the calcium level lower at the time of their break, as also the bactericidal efficiency of their blood, and that the records of their breaks show the following lesions: dental caries, kidney involvement, stroke, nervous breakdown, degenerative arthritis, neuritis, and various of the sensitization reactions of the skin, hyperesthetic rhinitis, asthma, or hay fever. The third group with the absence of susceptibility to rheumatic group affections, characterized by the marked rarefying osteitis with extensive decalcifying processes, tends to have a high blood calcium, both total and active. The bactericidal efficiency of their blood is high for streptococci, and while they have the sensitization reaction, and periodontoclasia, they largely furnish the individuals with diabetes, tuberculosis, cancer, and certain of the anemias.

We have made chemical analyses of the blood of over 1200 typical individuals of these groups, and while it is impossible to be exact in the matter of classification, the figures strongly indicate a marked tendency to differences of calcium level in the individuals of these various groups at the time of our making our observations, which in the second and third group would be largely at the time, and frequently because of the recognition of the patient's untoward symptoms. These individuals would show a different calcium level at other periods. An average of a series of each of these three groups is shown in figure 19, in which it will be seen that group I, in whom the resistance is high, tends to have both a high total and a high active calcium, namely, an average of 11.9 for total and 10.5 for active calcium. In group II, with mild breaks, there tends to be a high total and low active calcium, 11.2 and 9 respectively. In group III, with severe breaks, the total calcium averaged 9.5, and the active 8. This does not include severe conditions such as osteomy-

elitis. In one case the total calcium was down to 8.5, with non-diffusible or colloidal calcium at 1.2, and in another the total calcium was down to 8.7 and the active to 7.9.

I have now accumulated a mass of data which is consistent in its general uniformity and which because of its apparently great significance and importance, I am putting in the form of a monograph, it being too voluminous for inclusion in technical research reports. These data strongly indicate that the injurious effects of dental infections

A.—GENEALOGICAL TREE (HURST)



Cases suffering from nephritis are italicized.
* Has had attacks of epistaxis and hematemesis.

FIG. 18. GENEALOGICAL TREE OF FAMILY WITH NEPHRITIS
Total number 28; affected 16

upon the defensive factors of the blood, and upon the disturbance of its normal levels, particularly of calcium and its compounds, have not been adequately emphasized. These effects, constitute one of the most important, and probably the most important disturbance produced by them. When an infected tooth is placed beneath the skin of a rabbit, it practically always produces one of two conditions—either the foreign substance is surrounded by a highly vascularized defensive membrane which constitutes an efficient local quarantine, temporarily so at least, or a series of changes take place in the blood, which I have indicated previously, namely, depression of the polymorphonuclears, increase of the small lymphocytes, depression of the active calcium, and often of the total calcium. I have also stated that when the active calcium decreased to about 5 or 6 mgm. the animal goes into spasms and usually dies in a short time. Prior to this crisis, there is a marked increase in sensitiveness or nerve reflexes and sometimes tetany. We, of course, do not get this extreme picture in humans. We do, however, find many individuals who, for long periods are in a state of disturbed calcium balance. The limited time does not make possible the presentation here a mass of evidence which is available for supporting the above thesis. I will, therefore, be able to present only a few limited illustrations, from both experimental and practical cases.

Figure 20 shows a graph of the consolidated story of the inoculation of rabbit no 1356 by putting an in-

fected tooth beneath its skin at which time the total calcium (1) stood at 13.9 mgm.; the active calcium (2) at 10.5 mgm.; non-diffusible (4) at 8.4 mgm.; diffusible (5) at 4.9 mgm.; inorganic phosphorus (3) at 4.5 mgm.; total calcium balance (7) at plus 21 mgm.; (the product of inorganic phosphorus and total calcium minus 40) the active calcium balance (8) at plus 8 mgm.; (the product of active calcium and inorganic phosphorus minus 40). The horizontal line on the chart represents 40, and the figures above and below this line represent positive or negative calcium balance. The weight line which is represented by increase or decrease above or below the starting point, 2200 gm. is shown in (9) and the leucocytic count, starting at 7000 in graph (10). The heavier perpendicular lines of the squares represent number of days, and the heavier horizontal lines milligrams per cent. It will be noted that in the first five days, after the infected tooth was placed under the skin of the animal the total calcium decreased from 13.9 to 12.5, during which time the active calcium decreased from 10.5 to 6.2; the inorganic phosphorus decreased from 4.5 to 3.4; and the calcium balance for both total and active accordingly dropped rapidly. All animals and all individuals whose calcium balance lines are below the base line are presumably in a pathological state. In over 200 rabbits studied by placing an infected tooth beneath the skin, 75 per cent have died as I have stated when the active calcium decreased to the vicinity of 5 mgm. This rabbit was at the end of seven days, therefore, in very grave danger. The active calcium balance stood at minus 22. According to the history of previous cases, the animal would soon have been dead. At this point, an injection was made of parathyroid extract, at which time, the leucocytic count, which had gone up during the first four days, was receding. It will be noted that with the three injections of our own preparation of parathyroid by the method of Collip, which increased the solubility factor of the blood for calcium, all the graphs rapidly moved upward, the total going from

Table 13. Average calcium levels of three typical health groups of eleven each on the basis of blood chemistry.

	ALKALINITY INDEX	TOTAL CALCIUM	ACTIVE CALCIUM	INORGANIC PHOSPHORUS	TOTAL ORGANIC PHOSPHORUS	TOTAL CALCIUM BALANCE	CALCIUM ACTIVE BALANCE	SUGAR	NONPROTEIN NITROGEN	CHOLESTEROL	TOTAL FATS	FATTY ACIDS
Group I. Resistance high; high total-high active.....	34.3	11.96	10.59	3.2	41.5	−0.3	−4.8	108	27	139		
Group II. Mild breaks; high total-low active.....	33.4	11.25	9.02	3.0	39.5	−5.5	−13.0	139	32	143		
Group III. Severe breaks; low total-low active.....	36.3	9.58	8.07	3.0	58.6	−12.6	−14.6	101	29	112		

FIG. 19. THREE GENERAL TYPES OF BLOOD PICTURE

Group I, high total, high active calcium; group II, high total and low active calcium; group III, low total and low active calcium.

12.2 to 14.4, the active from 6.1 to 8.2; the calcium balances both changed. The leucocytic count improved but this improvement was temporary. The rabbit soon began to decline. With this temporary improvement, at which time calcium was being taken from the bones through the increase in the solubility factor of the blood for calcium, there was a marked loss in weight of the animal, coincident with the improvement in the clinical picture. The fuel for the defense was secured at the expense of the body tissues. At this point, to check the further decline, and in order to pay the calcium bill from without, activated cod liver oil and calcium lactate, on two days in succession were placed in the rabbit's stomach by tube, as shown at the point of the arrow on the ninth day. Again there was a marked improvement in the calcium balance, largely through the reinforcement of the metabolism of inorganic phosphorus. This improvement was again temporary. Note that the total calcium came down progressively, at the figure marked (11) following the administration of parathyroid, but with the administration of the activated cod liver oil and calcium lactate, the active calcium came up rapidly to 10.2 approximately its starting point. The rabbit was still carrying the infection, and a quantity of pus, making an abscess about as large as a hen's egg, had accumulated around the tooth. Ultraviolet irradiation was given on three successive days, at the point marked (12) on the total calcium line. Note the increase shortly after this in the leucocytic count, which jumped from 9000 to 28,000. With this splendid defensive reaction, the size of the accumulation about the tooth decreased from the size of a hen's egg as previously to about the size of a hickory nut so that the pus was no longer palpable. Note that the calcium balance for both total and active calcium passed well above the base line; the total calcium again mounted to and above its original normal, 15.3; the tissue over the tooth broke down and the tooth was exfoliated and the animal was out of danger. At the time of this writing, six months after the above experiment, the animal is apparently still in good health. Space does not permit the inclusion in the graph of extension of the lines to the time of the exfoliation of the tooth.

At the same time that this experiment was run, in fact the inoculations were made simultaneously, a similar one was made on another rabbit, no. 1357, as shown in figure 21. In general the charts started out the same, except that with the less rapid decline of the active calcium, as shown again in line (2) there was an increase in the total calcium, instead of a decrease. The calcium balance lines both go rapidly down, since the infection has greatly disturbed both the active calcium, and the inorganic phosphorus levels. Note that in this case, the non-diffusible calcium has steadily advanced. The injections of parathyroid correspond with those in the previous chart, and the results are similar with the administration of activated cod liver oil and calcium lactate. Note that the leucocytic count increased from 11,000 to 20,000 with the injection of the parathyroid, thereby gaining 9,000, and with the administration of the activated cod liver oil, and the calcium lactate, increased from 12,700 to 24,000, then falling rapidly to 13,000. During all this time the total calcium kept well above its starting point. The calcium balance lines which show the marked improvement at the time of the boost

given with the parathyroid and activated cod liver oil, started downward again, but were temporarily turned back toward the zero line, with the use of ultraviolet radiation, by a change in the direction of the various levels and the animal rapidly progressed toward its normal as shown by the upward direction of practically all the lines. Note

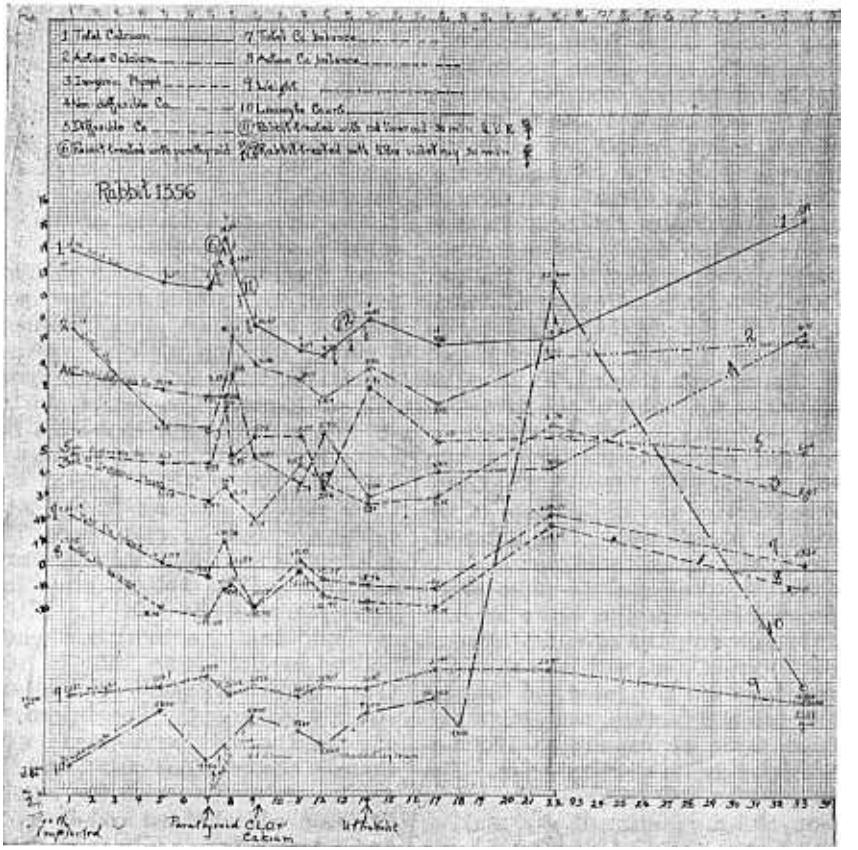


FIG. 20. CHANGES PRODUCED IN VARIOUS BLOOD FACTORS BY PLACING INFECTED TOOTH BENEATH THE SKIN OF THE RABBIT

1, total calcium; *2*, active calcium; *3*, inorganic phosphorus; *4*, non-diffusible calcium; *5*, diffusible calcium; *7*, total calcium balance; *8*, active calcium balance; *9*, weight; *10*, leucocyte count (rabbit, no. 1356). Note marked changes, especially of active calcium and response to treatments.

and then started downward. At this point, the pus was evacuated surgically and the tooth was removed. This was promptly followed particularly the decrease in the weight line, until the tooth was removed, and then its steady increase. I have much data on these various

problems which I interpret to indicate that the increase in the total calcium level is a mechanism of nature to maintain or to draw upward the lowering active calcium level. These data in support of this consist not only of many animal records, similar in many phases, to these two protocols just cited, but also many practical cases from practice which will be typically illustrated by the following.

Figure 22 gives the condensed summary of important calcium changes and the effect of treatment upon the same. This patient had several dental infections, and had a cellulitis develop, following extraction under gas. We do not have the details as it was done in another city. He had been a semi-invalid, unable to carry on his business, for a couple of years. In connection with the removal of further dental

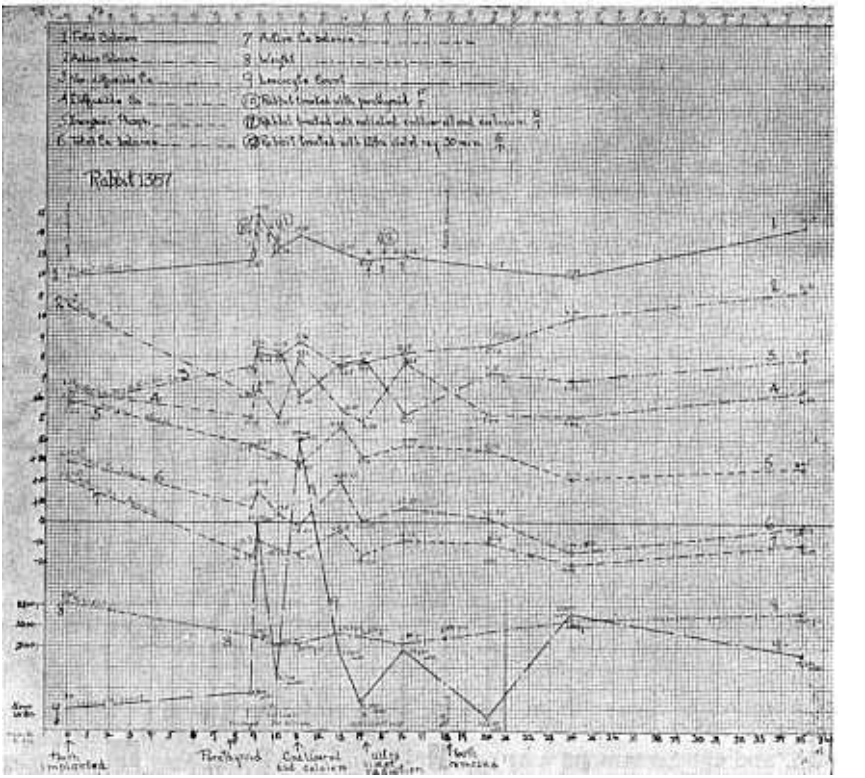


FIG. 21

Similar treatment to that shown in figure 20 was given. The tooth was less toxic. Note rise in total calcium with fall of active calcium and rapid improvement with removal of tooth. *1*, total calcium; *2*, active calcium; *3*, non-diffusible calcium; *4*, diffusible calcium; *5*, inorganic phosphorus; *6*, total calcium balance; *7*, active calcium balance; *8*, weight; *9*, leucocyte count (rabbit no. 1357).

blood and body tissues, and it is my belief that this constitutes the most frequent, and in total, the most serious expression of dental infection. When an infected tooth is placed beneath the skin of a rabbit, with the depression of the active calcium, there is a marked reduction in the rate of motility of the leucocytes, which is readily disclosed by placing a capillary tube, containing infected culture medium with its open end underneath the skin. The leucocytes have been shown to migrate only ½ inch in two hours, when the calcium is depressed 20 per cent, and

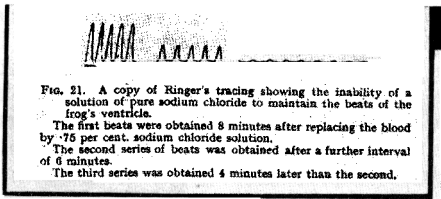


FIG. 21. A copy of Ringer's tracing showing the inability of a solution of pure sodium chloride to maintain the beats of the frog's ventricle.
The first beats were obtained 8 minutes after replacing the blood by ·75 per cent. sodium chloride solution.
The second series of beats was obtained after a further interval of 6 minutes.
The third series was obtained 4 minutes later than the second.

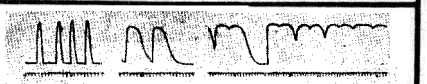


FIG. 22. A tracing (from Ringer) to show the effect of calcium salts in favouring the contracted condition of the ventricular muscle.
The first beats were obtained while the heart was perfused with blood.
The later groups of beats were obtained after the replacement of the blood by sodium chloride solution containing a little calcium.

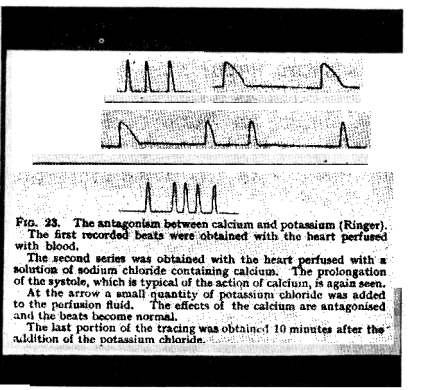


FIG. 23. The antagonism between calcium and potassium (Ringer).
The first recorded beats were obtained with the heart perfused with blood.
The second series was obtained with the heart perfused with a solution of sodium chloride containing calcium. The prolongation of the systole, which is typical of the action of calcium, is again seen.
At the arrow a small quantity of potassium chloride was added to the perfusion fluid. The effects of the calcium are antagonised and the beats become normal.
The last portion of the tracing was obtained 10 minutes after the addition of the potassium chloride.

FIG. 23. EFFECT OF PRESENCE OR ABSENCE OF CALCIUM ON HEART MUSCLE CONTRACTION

upon injecting calcium lactate either subcutaneously or by rectum, as suggested by Hamburger, or by placing calcium lactate and cod liver oil in the stomach the rate of migration has been notably increased in two hours time. A very common clinical improvement in the removal of dental infection is the decrease of lassitude, and in heart cases, the removal or decrease of sensations about the heart.

Nerve irritability has been abundantly shown to be very directly related to the concentration of calcium ions. The tetany of parathyroidectomized animals is preceded by a hypersensitiveness of nerve response, progressing to extreme irritability as convulsions and tetany approach. These are readily relieved by the administration of calcium.

An analysis of over 1200 human blood chemical studies, with special consideration of calcium factors, in relation to dental infections has presented much evidence indicating similar changes to those found in animals in which chronic focal infection has been established and similar improvement has followed the removal of dental infections. A typical illustration will be seen in the following: This patient at sixty-one years, presented with one of his chief symptoms, nervous irritability and lassitude. With the removal of his dental infections the alkalinity index of his blood increased in twenty-five days from 33.4 to 36 (40 to 45 being normal); total calcium from 9.7 to 11; active calcium from 8.5 to 9.4; inorganic phosphorus from 3.5 to 4.1 and non-protein nitrogen reduced from 40 to 30. With the removal of the dental infections and coincident with the return toward normal of the calcium

factors, this man experienced a very marked improvement and rapid return to normal health.

We have many times noted a characteristic irritability of the heart show marked improvement with the removal of the dental infections, and coincident with the improvement of calcium levels. When the writer's calcium is depressed, he can recognize the condition by the irritable way in which his heart does its work, and when the blood calcium is normal he is not conscious that he has a heart. Of course, many other factors than dental infections may disturb calcium levels.

To summarize I would state that the accumulating evidence strongly stresses the importance of focal infections such as a dental focal infections, being an important contributing factor to degenerative disease, and that one of the most important aspects is to be found in the direct effect upon blood stream changes, particularly of calcium levels, and thereby upon the function of various organs and tisues. It is further strongly indicated that disturbances of calcium cannot be estimated by determining simply the total calcium, which factor may be increased instead of decreased as part of nature's mechanism to hold up certain depressing constituent calcium factors. If ultimately we are to provide preventive measures, it seems very strongly indicated that we shall eliminate focal infections before there is systemic evidence of their presence, as clinical lesions. This does not mean that when in doubt all teeth should be extracted, but it does mean that more careful distinction must be made to determine what is, and what is not, a contributing dental infection.

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