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Focal infection""

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"FOCAL INFECTION"

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INTRODUCTION

It is my object in writing this paper to correlate the experimental and clinical findings on focal infection. In reviewing the literature, it was found necessary to eliminate many articles which seemed to deal too much with specific problems of focal infection. A great deal of stress will be placed on the theory of elective localization of bacteria as this seems to be closely linked with the controversy over focal infection. Much of the work on the problem has been done by E. C. Rosenow and his associates or by men trained in his laboratory. The clinical problem has been discussed by many clinicians from all specialities and by the general practitioners. The great bulk of literature on the clinical problem makes it necessary to exclude much of it from this review as it would entail much repetition. It is the hope of the author to find some base line for the evaluation of the importance of focal infection in the practice of medicine as a result of the experiences and experiments of clinicians and technicians for the past thirty-three years. No attempt will be made to analyze the occurrence of specific diseases or specific locations

of foci in the body. Only a consideration of the general problem of focal infection will be undertaken.

In order to eliminate some of the controversy, a clarification of terms seems to be in order. Infection means the invasion of the body by micro-organisms that have the power of reproduction in the host, of producing reactions in the tissues of the host, and the reaction producing abnormal phenomena which are termed clinical manifestations of disease. A focus of infection differs from a focal infection. A focus of infection may give rise to focal infection or it may give rise to intoxication of the body. Focal infection means the invasion of the body from a focus of pathogenic organisms, and these organisms have the power of reproduction or multiplication within the host.[7] A focus of infection is a chronic, usually low-grade, infection that develops insiduously and progresses slowly, producing symptoms of local and systemic disease.[22] It seems to be the site where the micro-organisms can attain specific pathogenicity chiefly in the nature of tissue trophism.[6, 8]

The theory of focal infection is not new. C. H. Mayo cited Hippocrates as having recorded two cases in which eradication of infections of the

mouth had relieved patients of rheumatic joints.[27] Several other early writers had made similar observations, but it remained for Frank Billings, in 1912, to set down our present conception of focal infection and its relation to systemic disease.[4] It was he who first related definite foci with specific systemic disease. He stated at that time that removal of foci was not the solution to therapy of these disease conditions, but rather was one of the factors in therapy. He concluded his article by stating that further work was needed on this subject. He followed this paper in 1914 with a further review of the principles and factors involved in focal infection. He stated that "the focus of infection could be found anywhere in the body, but usually in the head". The most common bacteria isolated from the tissues and exudates were Streptococci, Staphlococci, and Pneumococci. He believed that the oxygen tension around the focus seemed to be an important factor in the transmutation of the organism. In consequence of this, he believed that the organism may take on characteristics which make it "pathologically specific for various tissues

in the body when bourne by the blood stream". "The organisms were probably blood bourne as shown by histologic examination of the involved tissues which showed embolic bacterial masses in the terminal arteries. Endothelial proliferation at the site of the embolus closes the vessel lumen, followed by a localized anemic necrosis which provides ideal media for growth of the bacteria. Lessened nutrition and oxygen to the infected tissues brings about the characteristic results. Furthermore, the strains of Streptococcus which apparently cause a type of deforming arthritis and myositis grow best in low oxygen tension. The method by which they invade the tissues produces a condition in which they can thrive. A characteristic directly opposite is evidenced by Streptococcus Viridans isolated from a chronic infectious endocarditis. Here the infection is evidently hematogenous. The scar of healed endocarditis or valvulitis is often predisposing. The circulating blood furnishes the high oxygen tension needed by the organism. Here the organism multiplies and becomes immunized to the resistance of the host. This shows the difficulty of treating

these cases clinically." They propagate themselves by the environment they have created.[5]

Billings believed that an important predisposing factor to focal infection is diminished bodily resistance which may be caused by colds, overwork, poor hygiene, alcoholism, poor nutrition, and dissipation in general. Removal of the focus prevents further inoculation of the focal point. It will not, however, cure the condition, but will only aid in the treatment of the condition. In some cases general bodily resistance may be built up to throw off the infection after the source is removed.[5] He further believed that most of the common pathogenic bacteria had the "biochemical power which permitted them to exist in the host as harmless parasites or vicious pathogens". The varying pathogenic qualities, special and general, may apparently be acquired in the host or in the passage from host to host or in culture media. This may be due to variations in oxygen tension in various tissues in the host or culture media. The special or general pathogenicity of the infectious agents of the focal infection, and the

susceptibility of the host may determine the severity and extent and the site of systemic infection.[6]

In 1915, E. C. Rosenow published his first work on the theory of elective localization. In his experimental work, Rosenow used Streptococci isolated from foci of infection found in patients with such diseased conditions as appendicitis, gastric and duodenal ulcer, cholecystitis, rheumatic fever, erythema nodosum, herpes zoster, epidemic parotitis, myositis, and endocarditis. The Streptococci were grown for 16 to 24 hours in ascitic broth fluid at 37 degrees F. The cultures were then injected intravenously into rabbits and dogs, the dosage varying with the size of the animal. He believed that the tendency to localize was more highly developed in the relatively non-virulent strains from chronic foci, while the virulent strains produced more widespread lesions. The changes observed, such as cloudy swelling, hemorrhage, and necrosis from a chemical viewpoint, are similar to changes observed in simple tissue asphyxia. He believed that since bacteria are powerful reducing agents, they may act chiefly by

interfering with cellular respiration and possibly the greater the virulence the greater the interference.[47]

In 1916, E. C. Rosenow published further work on elective localization of bacteria. It was done on a patient with myositis and dental neuralgia. The focus was found to be pulpitis. His experimental animals were rabbits, dogs, and mice. Using sterile technique, he cultured the pulp of the infected tooth in deep glucose brain broth which supplied a range of oxygen tension from anaerobic conditions at the base to aerobic conditions at the surface. The micro-organism isolated was a Streptococcus. The cultures were then injected intravenously into the rabbits and dogs, and intraperitoneally into the mice. The animals were autopsied, and it was found that localization took place around the dental nerves and in the muscles of the neck. This corresponded to the site of the patient's symptoms. The Streptococcus was demonstrated in the sections and isolated from the infiltrated deep fasciae and muscles of the left side of the neck of the animals. This Streptococcus was

isolated and reinoculated in other experimental animals. This was done repeatedly and it was found to have an affinity for the muscles of the neck and the dental nerves. Streptococci from other sources failed to show this tissue affinity. It was also noted that the phagocytic power of the patient's blood following the attack was about two times that of comparable normal blood on the strain of Streptococci isolated from the jaw.[48]

Rosenow and Ashby published further experimental work on focal infection and elective localization in myositis. In this series the 28 patients selected had symptoms of myositis. In this group, 25 had demonstrable foci which were removed, 24 received relief. Cultures were taken from all foci removed and were injected intravenously into rabbits. In the experimental animals, muscle lesions were found from 24 of the cultures. These were from patients who had gained relief following removal. On microscopic section of the involved muscles from the rabbits there was found a round cell infiltration which helped to occlude the blood vessels in the area. From this evidence they decided that there was an altered oxygen tension on the cell which thus

favored growth of the bacteria in that location. This is the response which is often seen in chronic disease processes and was thought to be a factor in the growth of specific types of bacteria. This explains Rosenow's insistance that culture media must be used, which give a range of oxygen tension, when culturing various foci. He believes that alteration in oxygen tension caused by culturing the organisms on standard media causes a change in virulence and a change in tissue affinity of the involved organism.[51]

Aaron, in 1919, brought out several factors relating to the clinical aspects of focal infection. He believed that susceptibility to infection was not only due to the physical state of the exposed individual, but also to his habits, diet, occupation, age, environment, climate, and sex. He also believed that secondary metastases were dependent on mutation in bacteriological pathogenicity of the Streptococcus-Pneumococcus group. These variations in the two groups was first discovered in the laboratory, but is believed to take place also in the tissues of the human. The tissues act as a culture media. This is thought to

take place in a localized focus and the more virulent bacteria disseminated from here. Blood supply, oxygen tension, and unknown biochemical factors are all thought to be operative in the focus and modify or entirely change the characteristics of the bacteria brought there. This would explain the sudden flare-up of a lesion from some chronic focus.[1]

In 1920, Billings, in discussing a paper presented by Fontaine, declared that much of the failure in the treatment of focal infection was due to the fact that the practitioner removes the focus, but then fails to treat the condition for which the focus was removed. He stated that "if you have removed the focus you have merely prevented the further invasion of the tissues by new organisms". Focal infection is usually an invasion of the tissues by pathogenic organisms through the blood stream. They lodge in the tissues and produce reactions dependent on their character and virulence. They remain in the tissues as long as the defenses of the host are not strong enough to kill them or drive them from the body.[7]

In 1920, Fontaine stated that failures in treatment were often due to a wrong diagnosis. He states that often the relation of a focus of infection to the symptoms in question had depended on 1) the absence of any other demonstrable cause for the symptom, 2) the failure to cure the symptom by all other means of treatment, and 3) prompt and continued relief with no return of the symptoms, or the cure or eradication of the foci of infection. He urged a more thorough study of the patient before diagnosing the disease as due to a focus of infection.[20]

In 1921, Rosenow published two more articles which tended to confirm his previous experimental work. In the latter article[50] he brought out that Streptococci having elective affinity had been repeatedly isolated from pulpless teeth that did not show rarefaction at the apices on x-ray studies. He stated that "just as certain types of Streptococci tend to remain localized to particular areas in the throat, such as hemolytic Streptococci to the tonsils, so strains having specific localizing power tend to remain limited to the focus". Experiments indicated that while the different strains

of Streptococci in a given disease have specific infecting power and other properties, they may become sufficiently modified under the influence of changed environment to be the cause of different diseases. Rosenow stated that the reasons for the presence in the foci of bacteria having specific localizing power, possibly in part due to peculiar environment afforded by the tissues, was still obscure.[49, 50]

In 1922, DeNiord and Bixby published some findings on laboratory work which they believed would aid in diagnosis. They stated, however, that under the term "focal infection" they included chronic accumulations of pus, and areas exhibiting an abnormal degeneration of the cellular elements enclosed in any of the cavities or tissues of the body. They believed that in focal infection there was nuclear degeneration with a resultant increase in blood uric acid levels. Other conditions giving high uric acid levels are leukemias, primary anemias, cachexias from various causes, and massive doses of x-ray or radium. These conditions should be ruled out before considering focal infection. In their work they found

that the elimination of all foci of infection invariably was followed by a return of the uric acid level to normal. Further, failure to eliminate all foci will prevent the return to a normal uric acid level, and they believe that this may be used as a criteria for the complete eradication of foci.[14]

In an attempt to simulate conditions as actually found in clinical practice, Rosenow and Meisser in 1922, working with dogs as the experimental animal, devitalized and infected several teeth in each animal to determine elective localization from a circumscribed focus. The dogs were all selected, and under sterile technique, the crowns and pulp from several teeth were removed. Then the teeth were inoculated with cultures from foci removed from patients with nephritis. The teeth were then sealed with metal amalgum. After several weeks, the dogs were autopsied and it was found that the kidney contained lesions resembling a focal nephritis. The organisms cultured from the kidney bacteriologically were the same organisms as inoculated into the pulp of the teeth. Another group of animals were selected and inoculated intravenously.

These animals also showed lesions in the kidneys. Pathologically the kidneys showed extensive interstitial infiltration by large and small round cells. This closely resembled an acute interstitial nephritis. The dogs showed no "clinical" signs resembling those found in humans, but probably would have if given time. They concluded that these experiments are convincing proof of elective localization of bacteria from a focus of infection.[52]

Barnes and Giordano, using bacteria removed at postmortem, attempted to prove Rosenow's theory of elective localization. In the experimental work, bacteria were recovered from various locations at necropsy including various foci of infection. These cultures were then inoculated into experimental animals. Thirteen morbid conditions comprising cases of nephritis, gastric ulcer, encephalitis, and primary peritonitis were studied. Eleven of these conditions were produced in the experimental animals by intravenous injection of the cultures. They stressed the early discovery of foci and their removal if satisfactory results are to be expected. They believe that a long continued insult may result

in irreparable damage or a self-perpetuating process in a given structure.[3]

C. H. Mayo, in 1923, stated that in his opinion the elective affinity of the Streptococcus often causes disease by inciting conditions necessary for their formation.[34]

A. D. Dunn, in 1923, stated that in his opinion the excess load factor caused by the focus had not been sufficiently emphasized. He believed that focal infection was often responsible for the chronic fatigue or "rundown" states with which the practitioner is often confronted. "Two big reasons for removing foci are 1) the closure of a door of entrance into the circulation for infecting microorganisms and their toxins and 2) the removal of a useless load which the system is compelled to carry."[17]

Wootton, in 1924, in discussing the theory of focal infection, stated that he believed many failures clinically were due to 1) pathological conditions in near borderline cases not recognized, 2) incomplete physical examination, 3) the disinclination for radical procedures in the absence of gross lesions but with active symptoms, 4) discouragement

following removal of one obvious focus with no relief of symptoms, 5) the confusion between past results and continued infection, 6) the removal of primary foci with no attention to the secondary foci, and 7) failure to locate possible foci after an exhaustive search.[63]

Haden, in 1925, using rabbits for his experimental animal, studied 12 cases of peptic ulcer from the standpoint of a possible causal relation of dental infection. He made cultures from the teeth in glucose brain broth to provide optimal oxygen tension. The organisms recovered were pure Streptococci or Streptococci associated with Staphlococci. Of 45 rabbits injected intravenously with the cultures from the 12 cases, 53 percent showed gross lesions of the stomach or duodenum at necropsy. As a control, 191 patients with foci of infection but without signs of gastric or duodenal lesions were cultured and these cultures injected intravenously into 535 rabbits. Only seven percent of these cases showed lesions of the duodenum or stomach. It was noted that in the 45 rabbits injected with cultures from patients with peptic ulcer, the great majority of lesions of the duodenum were confined to the duodenal bulb.[25]

F. A. Faught believed firmly in the radical extraction of foci stating that the cure rate makes up for the teeth and tonsils sacrificed. He states that an important cause of failure in therapy is due to the "physical inadequate". These are the types of patient who are unable to throw off an infection in spite of adequate therapy. He also cited the danger of multiple removal of foci at the same time. This seems to cause an acute flare-up of symptoms probably due to the stirring up of the nidus of infection with liberation of toxins or bacteria.[19]

In 1926, J. A. Kolmer wrote that in his opinion elective localization of bacteria was not a sound theory. He believed rather that there was a pattern of distribution based on local tissue immunity, local trauma, and blood supply. This, he believed, explained why some can hold a focus of infection without secondary involvement. He states that soluble proteins from the bacteria in the focus may be absorbed and set up an allergic state in some distant organ or tissue. The exacerbation of symptoms in a secondary focus following manipulation of the primary focus is strong presumptive evidence for focal infection.[30]

R. S. Morris is convinced that the removal of foci is important even in advanced cases, for in his experience it has slowed the course of the disease considerably. The prognosis in all the cases studied was in large part dependent on how early treatment was instituted and how much permanent damage had been done.[36]

Pemberton, Cajori, and Crouter in 1926 advanced a new idea on the influence of focal infection on systemic disease. Their studies were on arthritic patients. Under suitable conditions of "load", the arthritic patients have been shown in 60 percent of cases to remove certain constituents from the circulating blood, namely, oxygen and glucose, with less than normal rapidity. This phenomena closely parallels the incidence of focal infection. Among the 40 percent of arthritic patients who did not show this delay, it was induced, in respect to glucose, by interfering with the blood flow of the limbs in half the cases studied. This delayed removal was therefore present actually or potentially in 80 percent of the total number of cases studied. They were unable to induce it in normal patients. In the 60 percent which actually showed this

phenomena, it could be restored to normal by vasodilators. They could not definitely explain these observations but thought it might be explained on the basis of vasoconstriction which may have been induced by toxins from a focus of infection.[44]

Murray tried to explain the various ways in which a focus of infection could influence or initiate some disease process. In the first place, bacteria may be discharged and conveyed by mechanical means so as to cause extension of the disease by re-inoculation. Secondly, the bacteria present in the original focus may overcome the local resistance and be conveyed by blood stream or lymphatics to distant parts of the body. Once the bacteria leave the focus, either singly or in groups, they may be arrested by the nearest lymph gland and set up a lymphadenitis which may develop into an abscess. If the infection passes the lymph gland, three things may happen: 1) if the organisms are virulent, they may multiply and set up an acute or chronic septicemia, 2) if they do not multiply in the blood, they may be conveyed alive to suitable tissues where they multiply and infect the surrounding tissues, and 3) if the bacteria conveyed by the

blood are unable to gain a real footing anywhere, they may produce a slow but progressive atrophy with replacement fibrosis in various organs or tissues of the body. Thirdly, the micro-organisms may remain enclosed at the seat of the focus of infection from which their toxins are continuously absorbed so as to cause either temporary alteration in the structure and function of the blood and other tissues, or possibly permanent structural change in important organs.[39]

Nickel, after considerable experimentation in 1926, made several observations. Paramount among these was the fact that certain bacteria, usually Streptococci, freshly isolated from foci of infection, tend to produce lesions in experimental animals corresponding to those lesions in patients from whom they were isolated. It was found that the bacteria could be isolated from single or multiple foci in the patient as the case may be. Also it was noted that the incidence of specific localization was highest in cultures from the teeth. Aside from such factors as injury or fatigue, the inherent property of bacteria to localize

electively in certain tissues determines largely the site of the disease in persons harboring foci of infection. This holds true not only for strains isolated in acute, but also in chronic diseases; and advanced changes have been produced experimentally following injection. Causal relationship between the organisms and the lesions produced was established through isolation of the former from the lesions when the blood and other tissues were sterile, and by their demonstration in sections. He believed that the method of determining localizing power could be used for diagnostic purposes as well as for therapeutics, by demonstrating which organisms in a foci are malignant and which are the benign ones.[40]

R. B. Canfield believes that the lymphoid tissues of the oral cavity account for 80 percent of the cases of focal infection recognized clinically. Before the age of five years, the removal of tonsils should be carefully considered as he believes that they act as a first line of defense against infection and possibly have some endocrine function. After the age of five, however, he believes they may be removed with impunity. In

his opinion, teeth and sinuses constitute the other 20 percent of foci of infection.[11]

In 1927, H. M. Walker stressed the action of chronic absorption of toxins on the capillary system. Under normal conditions, the capillary system is capable of a considerable functional response to metabolic requirements of the body. The capacity of the cells to carry on their activity is dependent on this flexibility of the capillary system. The chronic absorption of bacterial toxins is a factor which may cause modification of capillary control, and the early manifestations of ill health from the toxins may be accounted for by the lowering of the nutrition of the cell through this modification. The person with "inherent" instability of the capillary system will tend to show a more pronounced effect of the toxic absorption; one with a very stable system may show little or no effect of the absorption. This effect may possibly be due to the integral effect of the sympathetics and para-sympathetics on the vessels, and the maintenance of a proper balance between the two. The capacity for widespread reaction shown by the capillaries as in the idiopathies may explain

the widespread disease caused by a minute septic focus. He believed that non-specific protein therapy acts by stimulating the peripheral circulation.[60]

In 1927, Rosenow brought forth some concepts of focal infection and elective localization somewhat modified from his earlier views. He brought out the importance of drainage and its relation to foci of infection, believing that the harm which is prone to come from foci was directly proportional to the lack of drainage to the surface. The virulence of the bacteria was another factor, the more virulent strains needing a less gross focus for entrance, while the lower grade bacteria were the more important causative factor in the production and maintenance of a chronic disease process. The severity of acute infections seems to have been made worse by the presence of foci of infection and the incidence of complications made higher. His views on elective localization were changed from that of transmutation to that of a variety of strains being present. He believes that the various strains have various points of elective localization. Fatigue, alcoholism, trauma, and any factors lowering bodily health and resistance were

believed to be factors influencing the production of focal infection and elective localization. Failure to relieve many clinical cases was found due to multiple foci containing the same micro-organism and failure to remove all the foci. He believed localization to be on a biochemical basis, for the washed products of dead bacteria including their toxins also manifest specific localization in experimental animals. Referring to foci, he stated that in his experience practically all pulpless teeth, regardless of x-ray evidence, were infected and either potential or active foci of infection.[53]

W. L. Holman, in discussing elective localization, stressed the importance of peripheral circulation as a factor. He believed that after the bacteria entered the blood stream, those factors altering circulation and thereby influencing the nutrition of the cells, particularly the endothelium of the capillaries, were of prime importance. Dilatation of the capillaries would tend to facilitate the invasion of the tissues, but a sluggish circulation would permit the more invasive types of micro-organisms, such as Streptococci, to go through or produce local thrombi in smaller vessels.

Quiescence or movement of the tissues and the type of circulation are also factors. The survival of the bacteria after reaching their destination is dependent on their virulence or on the "inherent" ability of the endothelial cells in a given organ to destroy them. Removal of a focus may effect a "cure" by removal of the organism lowering general systemic health. Failure to effect a cure, on the other hand, would seem to indicate that the correct focus had not been removed or that the secondary focus is well established and irreparable damage done to the tissues and local circulation. He stated that in his opinion the specificity of bacteria had not been proven and that the evidence so far presented was open to individual interpretation and therefore limited in its application. He does believe that a certain amount of bacterial adaptation to its environment does take place, but, on the other hand, the factors on the side of the host are much more variable and probably more important. The answer to the question would probably lie in the latter approach rather than the former.[27]

Giordano published work in 1928 in which he again cultured various foci postmortem in glucose

brain broth and inoculated these cultures into experimental animals. His results show a high percentage of the animals exhibiting lesions similar to those in the host from which removed. He believes that there is definite evidence that the bacteria possess a selective localizing power.[21] His studies and results are comparable to those made by Rosenow, Irons, and Brown,[28] Moody,[35] Oftedal,[42] Detweilerand,[15] and others.

In studies concerning results of removal of foci carried out by Rosenow and Nickel evidence was obtained which seemed to indicate a hypersensitivity of the tissues to the bacteria or their toxins in a focus of infection. They based this conclusion on the observation that following a radical removal of a focus, many patients showed an acute exacerbation of their symptoms. This was probably due to the sudden release into the system of larger amounts of bacteria or their toxins due to the irritation of the focus. They stressed the importance of cautious removal of all foci to prevent these acute affairs.[54]

Cameron and Rae conducted experimental blood cultures on 100 apparently well subjects. The nose

and throats of all subjects were carefully searched for any foci of infection. All cultures were collected on the same day and the same batch of media was used for all tests. Six positive cultures were obtained, four Staphylococcus aureus and two diphtheroids. This result would seem to indicate that bacteria may be transiently present in normal subjects with apparently no ill effects. Such episodes could start a focus of infection or could be due to obscure foci not uncovered by the ordinary physical examination.[10]

In 1931, Hale discussing the swing away from the theory of focal infection, said many of the failures were due to one of three factors: "1) a focus may be present, but still not be the cause of the condition of which the patient complains, 2) the focus may be the cause of the disease, and yet be removed too late to do the patient any good, 3) many patients with a neurotic tendency will be benefited by any work that is done including removal of foci and yet come back with the same complaints months later". This latter causes many to throw the theory overboard. He believes it very important to consider all the possibilities of the

etiology of the disease at hand and treat all obvious foci.[26]

Lourie bewails the mass removal of tonsils as the result of insufficient knowledge of the etiology of the disease process being treated. He believes the results obtained are insignificant in comparison with the sacrifices involved due to the operations. He stresses the fact that in too many cases foci are being removed because we do not know the cause of various disease processes and have nothing else to do in the line of active therapy. He does not believe that the theory of elective localization solves the problem of focal infection or can be of much help in the treatment of many disease processes to which it is now applied.[32]

Richards, in 1932, presented his results on 306 cases with obvious foci of infection in which he studied the incidence of bacteremia following massage of the foci. The foci were massaged and blood cultures taken one hour and 24 hours later. A control was run before massage. Of the 306 cases, over 17 percent showed a positive blood culture after massage. The majority of those positive cultures were found in the one-hour specimen

and absent in the 24-hour culture. He believes that trauma is an important factor in causing bacteremia and the establishment of a secondary foci. Further, he concludes that many patients may harbor a foci of infection without developing secondary foci. Whether or not the patient does develop a secondary foci is probably dependent on the bactericidal character of the blood.[46]

Woolsey, in 1932, brought out the idea that the colon could be a focus of infection. He believes stasis in the colon to be an important factor in allowing absorption of toxins. He believes that foci of infection may be the factor which "overloads" the system and thus makes way for secondary invaders. The importance of removal of this burden is stressed.[62]

Jones and Newsom, working with 24 dogs, ran a series to determine the importance of foci of infection in producing fatigue and cardiac hypertrophy. Twelve of the dogs were used as controls and 12 were inoculated with a strain of Streptococci isolated from patients with a hyperplastic sinusitis and who showed cardiac hypertrophy. One canine tooth in the 12 dogs was, under sterile

precautions, cut off and the pulp cavity filled with the Streptococcus culture. The tooth was then capped with cement and metal amalgum. The dogs were fed well and housed well with an outdoor run. They were exercised for 15 minutes a day six days a week on a treadmill of a 20 degree incline at 4.5 miles per hour. The dogs were all put through this routine for six months, which is equal to three years in human life. The inoculated dogs showed a higher death rate and a much higher incidence of fatigue. Dental abscess was demonstrated in all the inoculated dogs. There were no other constant extra-cardiac structural changes. The hearts of inoculated dogs constantly showed very small vegetative or verrucose mitral and/or aortic endocarditic lesions, patchy parenchymatous degeneration, nuclear changes, increased diameter of muscle cells, and slight round cell infiltration. The stress and strain in the control dogs had no gross or microscopic effect.[29]

Evans believed that the secondary lesions in cases of focal infection were primarily due to "lowered vitality or resistance" of the tissues affected. This lowered vitality he believes to be

due to a defect in the "trophic influence" or to "reflex antidromic impulses". These antidromic impulses seem to upset the vascular reflexes and therefore cellular activity. The vascular reflexes he believes to be essential in maintaining sympathetic balance.[18]

Wood, Jensen, and Post conducted studies on the surface electrical potential of microorganisms isolated from 215 cases in which focal infection was suspected. The bacteria were isolated from the foci and cultured in glucose brain broth. Eighty-seven percent of the organisms were a Streptococcus. The cultures were then centrifuged and the supernatant liquid was poured off and the bacteria washed and suspended in conductivity water. A Northrop-Kunitz-Mudd assembly was used to measure the electrical changes on the suspended bacteria. A total of 1350 cultures were tested. It was observed that in certain conditions the bacteria possessed characteristic charges of negative electricity. Now if serum contains antibodies, these will unite with their specific antigen and in the opinion of Northrop, the bacterial cell will be coated with antibody globin which,

in turn, will lower the electrical charge on the surface of the bacterial cell. In order, then, to find antibodies in the patient's serum, it is necessary to take bacteria of known pathogenicity and known mobility which have a specific electrical potential and incubate with varying dilutions of the patient's serum. Then measure the electrical potential and note a change which would be indicative of specific antibodies in the patient's serum. This method would be of value in the experimental study of the importance of focal infection in specific diseases.[61]

In 1934, Pern pointed out the importance of a chronic focus of infection in the maintenance of focal infection. He brings out the importance of the blood as a bacteriocidal agent which would prevent the growth of bacteria in the various organs of the body. It is his belief that such processes are perpetuated by the constant new supply of micro-organisms from a distant focus. He believes many factors are responsible for apparent variations in the virulence of the specific organism. Of importance in this explanation is the transmutability of the Streptococcus. The fluctuating resistance of the host brought on by fatigue,

alcoholism, undernourishment, and trauma is a second important factor. Bacterial toxins may have one of two actions on the tissues. They may either increase the functioning of the cell, causing a hyperplasia or hypersecretion, or they may decrease and destroy cell function. This may be another factor in explaining the various phenomena seen with the same organism.[45]

Solis-Cohen believes many of the failures in therapy are due to the misconception which concentrates attention on the infected tissue rather than on the infecting bacteria. After removal of infected tissue and drainage of an infected cavity, often times bacteria remain in adjacent tissue where they continue to multiply and disseminate their toxins to distant focal points. The remedy, in the mind of Solis-Cohen, is the use of autogenous or specific vaccines as well as a general therapeutic regime which will build up the resistance of the host. Vaccine therapy frequently fails because of an improperly prepared and improperly given preparation, often lacking the antigen necessary to stimulate the production of antibodies capable of destroying the infecting bacteria and rendering their toxins harmless.[57]

Mullin pleads for more conservatism in the evaluation of the importance of focal infection. He believes too many diagnostic problems are treated as cases of focal infection when in reality they are not. He also stresses the importance of stabilizing the patient before removing foci. Too many patients sustain permanent damage by the removal of foci during an acute attack of the systemic disease.[37]

Cecil compares the life cycle of the theory of focal infection to the rise and fall of a "movie star". There has been too enthusiastic removal of suspected foci without thorough search for the etiological agent of the disease being treated. He believes that the results have not justified the sacrifice of teeth, tonsils, etc. that has taken place. He pleads for more conservatism toward foci with less intensive surgery.[13]

CONCLUSIONS

It seems probable that much of the confusion and dispute in the literature has occurred because of the difference in the usage of the term "focal infection", and because too many expected the theory to explain the etiology of the great class of diseases whose cause is unknown. Thus far, too much has been expected from radical removal and autogenous vaccines. The place of elective localization in the picture is still not clear. That certain bacteria do develop tissue affinity seems likely, but how or why these bacteria develop such an affinity has not been answered. Transmutability of bacteria does not explain the how and why. The use of various tests, viz., uric acid levels, oxygen-glucose tolerance, and electrical potential of bacteria may be useful in the laboratory but are of no practical help for the clinician.

It seems probable that foci of infection are responsible for lowering that unknown quantity, "bodily resistance", and may be responsible for metastatic lesions in other organs and tissues, but the foci are not the answer to therapy in the many conditions first described by Billings and Rosenow. That removal of foci of infection is

important in the therapy of chronic disease cannot be denied. Too many patients have received relief from this type of therapy. This type of treatment seems indicated when definite foci can be found in patients with a chronic disease process. A careful survey of the patient must be made before these steps are taken, however, and a direct attack made on the disease process in addition to removal of foci.

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