

CHANGING CONCEPTS CONCERNING ORAL SEPSIS.*

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It seems to me appropriate to consider on this occasion, the development of the important subject of the changing concepts concerning oral sepsis, the clinical and experimental observations upon which it rests, and the good that has already come from its application, and to estimate the benefit that may confidently be expected to accrue from it in the years to come. Moreover, since your commission has seen fit to present this award to me for efforts of my own in this field that bear so directly on dental problems, I may be pardoned for reviewing briefly results of my own studies, particularly the earlier experiments that led to the conception of the theory of elective localization, and to point out why investigators, aside from those who have worked with me, have, until recently, had difficulty in corroborating the experimental findings.

Nowhere in medical history is the value that comes from combined clinical observation and experimental inquiry better illustrated than in the development of our knowledge of focal infection. Notwithstanding the repeated suggestions made in previous years concerning the etiologic relationship especially between acute localized infection and grave systemic disease, the medical and dental professions as a whole remained indifferent until Billings and his co-workers made their clinical observations and correlated experimental studies on animals, demonstrating the importance of localized infections, even though small and symptomless, as common sources of various systemic disorders. The broader conception of this interrelationship, well expressed by the term "focal infection," may therefore be regarded as having originated in recent years. I count myself fortunate in having been associated with Dr. Billings, to have been able to participate in this earlier work in Chicago and to have had the opportunity to continue my investigations in conjunction with clinicians at the Mayo Clinic in Rochester.

Aside from affording information concerning the pathogenesis of a series of diseases formerly not well understood, the work gave medical science a therapeutic principle of the utmost importance. Numerous reports on the relief of symptoms following the removal of foci of infection soon followed. The scope of this influence may be judged by the volumi-

ous literature on focal infection that has since appeared throughout almost the whole civilized world. The benefits that have already accrued directly or indirectly are almost beyond enumeration. It is not surprising that much speculation and opinion, often insufficiently supported by facts, have been indulged in both by clinicians who often have little conception of the real significance of experimental studies and by purely laboratory workers who know so little of the clinical applications of their findings. All of the men who were associated with Billings and who did the experimental work had had both clinical and laboratory training and had intimate knowledge of the condition of the patient under investigation. Both types of study have value, but this could be greatly increased if the studies in this field could be made in collaboration or in closer cooperation. Such combined study is the crying need today, in the further working out of this problem. How much more might be accomplished if the many operators in the dental field, particularly root-canal experts, exodontists and dental surgeons, could correlate their clinical and radiologic findings with results of equally expert bacteriologic and experimental studies in animals than by attempting to evaluate the safety of the various procedures, such as root-canal work, by mere clinical observation, as is now almost universally done. It is a noteworthy fact that the results of my work in this field have been verified almost wholly by men who have had the necessary clinical guidance in the selection of material from patients, or who have had extensive clinical experience as well as a laboratory training.

The inability of certain investigators to corroborate my results would seem to be explainable on the ground of the improper selection of cases and material for study or of insufficient attention to technical details, as pointed out especially by Gay and Haden. The early results in studies on ulcer were corroborated by Hardt and Helmholz, those on iritis by Irons, Brown and Nadler, and those on cholecystitis by Brown. The elective localizing power of streptococci and colon bacilli from urinary infections has been demonstrated by Helmholz and Beeler. The results in the study of ulcer and arthritis have been fully corroborated, extended and controlled in my laboratory by Meisser, with streptococci isolated from infected teeth in the study of ulcer of the stomach and arthritis; by Nakamura with streptococci isolated from extirpated tonsils, and by Giordano with streptococci isolated from infected teeth and tonsils after the death of the patient. My methods have been used successfully in a study of the etiology of pyelonephritis and ulcerative eye

titis by Meisser and Bumpus; by Moenich in a study of the etiology of endocervicitis, in which she demonstrated that this condition is often due to partial-tension streptococci and may be a common cause of arthritis in women, and in a study of the etiology of chronic colitis by Bargaen. Price, working independently, has also reported corroborative results. The work on iritis and other disease of the eye, on ulcer of the stomach and on pyelonephritis, as concerns dental foci especially, has been verified and greatly extended independently by Haden. Through strict attention to technical details, he has even succeeded in producing onychia in rabbits with streptococci from foci of infection in patients suffering from multiple onychia, an example of extreme specificity.

Certain investigators contend that all infections are focal in character. It is true that this is often the case in the microscopic sense, yet there is a fundamental difference between an area of infection around the joint, as in chronic arthritis, for example, and infection in the jaw surrounding devitalized or diseased teeth, or the tonsils containing dilated crypts with a narrowed or plugged orifice or an encapsulated abscess, and which, for mechanical reasons, cannot heal or drain.

In the systemic or secondary focus, the number of organisms is usually small; whereas, in the primary foci mentioned, the number is usually large. Again, there are those who say, "Why care about infected pulpless teeth or other foci of infection since the mucous membrane of the upper respiratory tract, and especially of the intestinal tract, harbors millions of organisms?" It is well known that normal mucous membrane are relatively impermeable to micro-organisms. In order to make the analogy more nearly correct, I would venture to suggest that the nerve supply to various segments of the intestines be cut off and that certain parts be wholly or partially ligated. Indeed abundant evidence is already at hand in which systemic disease results from improper functioning of the intestinal tract from various causes, such as reversed peristalsis, kinks and adhesive bands, infected diverticula, and, especially, from an appendix whose orifice or lumen has become narrowed from scar tissue, the result of localized infection, or has become plugged by fecal concretions.

Clinical observations indicated that localized infections in certain structures, such as tonsils, teeth and sinuses, are more likely to be associated with systemic effects than those in other structures, such as the lung, in bronchiectasis, or the urinary tract, in cystitis and pyelitis. This may be due to a difference in the kind, number of invasive power of the bac-

teria in these locations or to peculiarities of the tissues harboring such foci. In general, it may be said that the harm which is prone to come from foci of infection is directly proportional to the lack of drainage to the surface. The more virulent the bacteria, the less they need a gross focus for entrance, and the lower their virulence, the greater the factor of focal infection in the production and maintenance of chronic disease. There is much clinical evidence indicating that foci of infection, as in tonsils, are often directly responsible for rendering attacks of acute infectious diseases more severe than they would otherwise be, and for increasing the incidence of complications, such as in diphtheria and scarlet fever. Foci of infection in the upper respiratory tract, as in the tonsils, may also be of epidemiologic importance, as is indicated by the suddenness with which the diphtheria-carrier state disappears after tonsillectomy. In fact, the question of focal infection in its broader sense is as wide in its scope and as difficult of proper application as is the practice of dentistry, medicine and surgery, combined. It cannot be applied by rule of thumb any more than can the healing art. A focus of infection that for mechanical or any other reason cannot heal or drain, that is teeming with organisms, often in mixed culture, must ever be considered not only as a favorable place for entrance but also as a good place for bacteria to maintain or acquire high and particular invasive powers. Clinical observations support these contentions, and experimental results have gone far to establish them. Thus, control experiments with cultures from the buccal mucous membrane, the surface of the tonsils and throat often proven negative, the animals usually remaining well entirely or relatively free from lesions; whereas, strains from the depth of the focus produced characteristic lesions. Moreover, direct experimental proof of this fact has been obtained in the production of chronic foci by the devitalization and infection of teeth in dogs. Strains from patients with arthritis, nephrolithiasis and ulcer of the stomach, having elective localizing power, often retained this property for many weeks or months in the periapical structures of the teeth so infected; whereas, several aerobic platings sufficed to destroy it completely.

THEORY OF ELECTIVE LOCALIZATION

The best proof of the etiologic relationship of a focus of infection to a given lesion is the production of the lesion in animals with bacteria isolated from the focus in the patient.

Through the use of special cultural methods in which due consideration was given the question of oxygen tension and the injection of animals with the freshly isolated strains,

extremely characteristic localizations were obtained with *Streptococcus viridans* from patients with subacute bacterial endocarditis, and with streptococci isolated from the joints of patients with rheumatic fever before the idea of elective localization occurred to me. The peculiar localizations obtained were considered due to different species of streptococci, rather than to peculiar temporary properties of different strains of the same species. It was not until ulcer of the stomach was produced in animals during my study on the transmutation of pneumococci and streptococci with "laboratory" strains that had attained a certain grade of virulence from successive passage through animals that the theory of elective localization took definite form. The long series of experiments in animals that have been performed since by myself, my pupils and independent workers leaves no doubt that the elective power of the bacteria in foci of infection largely determines the location of the systemic lesion or disease a person with foci of infection is likely to develop.

This statement should not be taken to mean that this always occurs independently by predisposing factors. Exposure, trauma and fatigue of certain structure, improper food and bad sanitation, lack of sunshine, alcoholism and other excesses, undoubtedly lower the threshold of local or general resistance and thus greatly increase the likelihood of elective localization of bacteria and other infective processes. Direct intravenous injection of bacteria that had grown in foci, such as those contained in small amounts of pus from tonsils, has often been followed by localization, with the production of lesions corresponding to those in the patient. Moreover, the specific affinity was sometimes so marked that it was not always necessary to give the injections intravenously.

This observation answers an objection raised regarding large numbers of bacteria injected in routine work. Introduction of the bacteria in suitable dosage into the peritoneal cavity, the trachea, the brain, the stomach or the rectum, or into the nasal cavity by packing the nose with gauze soaked in the culture, was followed by specific localization in certain instances, especially when the more virulent strains were used. This supporting the clinical observations that systemic disease is not always attributable to a demonstrable focus of infection.

In order to remove all doubt regarding the importance of latent foci of infection as an important factor in the production of disease, Meisser and I produced latent foci by devitalizing and infecting the teeth in dogs, thus closely simulating the conditions often inad-

vertantly induced in persons by dentists. Nephritis, nephrolithiasis, ulcer of the stomach, spasms of the diaphragm and other muscles, and chorea have been produced in this way with culture isolated from patients with these respective diseases, and in each instance the causal relationship of the organism introduced into the teeth to the metastatic lesion has been established by the demonstration of the organism in the lesions and focus and by the elective localizing power of the strains isolated. During the latter experiments, another important fact was noted: The bacteria in the induced latent focus of infection, besides producing the characteristic disease, appeared to exert general deleterious effects. The animals lost weight and became more susceptible to intercurrent infections, although they were kept under conditions identical with those of control animals. In other words, conditions of hygiene and diet that were adequate to maintain weight and health in normal dogs were inadequate for dogs with latent foci of infection. The harm, therefore, from improper food or sanitation may be greatly exaggerated by bacteria harbored in foci of infection; a point not yet sufficiently considered.

In my experiments, still other important facts have been brought to light. Streptococci having the same specific localizing power were demonstrated in more than one focus in the same persons simultaneously, and, in some instances, at intervals, in one or more foci, over a long period. These experimental facts are in harmony with the common clinical observation that persons affected with a particular disease, such as iritis, ulcer or arthritis, are prone to have recurring attacks of the same disease, which often tends to become chronic in character. In the light of these facts, the possibility that the tissues or fluids of the body afford the conditions on which the development of the peculiar localizing power of bacteria depends must be seriously considered. The hereditary tendency observed in some of these diseases also points in this direction, as does the repeatedly made observation that a higher incidence and more marked lesions occur in the character organ or tissues of animals infected with the organisms from foci at the time of acute attacks or during acute exacerbations in chronic affections than during quiescent intervals. Moreover, well-marked differences in the incidence and severity of specific lesions were noted at different seasons of the year, especially in chronic ulcer and arthritis. During the colder months, when exacerbations and an increased incidence of these diseases are so common, the incidence of positive results in animals was appreciably higher than during

the warmer months, when patients were relatively or entirely free from symptoms.

The fact that bacteria of the same species localize electively, depending on the degree of virulence or other acquired property, is no more remarkable than the fact that bacteria of different species tend to localize in particular organs or tissues. The loss of virulence of streptococci or other bacteria on artificial cultivation and its increase on passage through animals are well recognized. The change in localizing power likely occurs for the same reason.

The reasons for the elective localization of bacteria are still obscure. No doubt the same principles that determine the localization or pharmacologic action of chemicals and drugs apply here. Indeed, my experiments in ulcer of the stomach and epidemic hiccups strongly support this hypothesis. It was found that strains of the streptococci from patients with ulcer which had elective affinity for the mucous membranes of the stomach and which produced ulcer, on intravenous injections elaborated a poison of toxin within the bacterial cell and in the broth that had specific damaging effects. Injection of the washed dead bacteria and filtrates of actively growing cultures produced hemorrhage and ulcer of the stomach without inciting lesions elsewhere. Even more striking were the results following intracerebral injection of living cultures of the streptococcus from patients with epidemic hiccups, the dead bacteria, and filtrates of freshly isolated cultures.

In each instance, spasm of the diaphragm or other muscles was produced. Moreover, filtrates of nasopharyngeal washings and pus from tonsils at the time of attacks sufficed to provoke spasms; whereas, similarly prepared filtrates, after recovery, were without effect. Aside, therefore, from the specific attraction of tropism of certain bacteria, their localization and growth in certain tissues are dependent on the production of toxins or poisons that damage those tissues specifically. The specificity of some of the strains was so marked that intravenous injection in pregnant rabbits was followed by localization and lesions that were similar in fetuses and mother rabbits. The view held by obstetricians that foci of infection predispose to miscarriage or to the ill health of the fetus is supported by clinical and experimental findings. The far-reaching deleterious effects that focal infection may have even in conditions generally thought to be hereditary in origin are well illustrated by the work of Talbot, who says:

"The evidence tends to show that most congenital malformations which are the results of lack of embryonic development are not hereditary defects but acquired in utero;

that defects in development are due to injury to the placenta during the early weeks of pregnancy; that the injury to the placenta is due to maternal hematogenous infection of the blood vessels of the placental site, and that the source of the hematogenous infection is generally to be found in the teeth and tonsils."

PRACTICAL CONSIDERATION

The practical applications of the principles of focal infection and elective localization are fraught with many difficulties. Systemic diseases, once thoroughly established and often associated with anatomic changes that in themselves may continue to give rise to symptoms even though there are no organisms present, may continue after all evident foci are removed. The instances of cure or arrest of progress in systemic diseases by the removal of foci of infection are so numerous that search for and removal of all foci possible is indicated in almost every case of serious systemic disease in which there is good clinical or experimental evidence of focal origin. In a given case the variations in the invasive power of the bacteria, the wide differences in natural or acquired resistance to microbe invasion in different persons and at different times, the age and sex, the history of previous attacks, the duration and character of the disease from which relief is sought, and hereditary tendencies must all be considered in determining when, or whether, all or certain foci should be removed, or whether the condition is indeed of focal origin.

To arrive at a correct diagnosis and to manage focal infection properly often requires the advice of specialists in the various branches of the healing art, as well as that of a competent bacteriologist. The opportunities of the dental profession have been greatly increased through a better understanding of the problem of focal infection in general, and especially of the dental area. Many problems are still unsolved, but enough have been solved to prove that prevention and elimination of oral sepsis should henceforth take precedence over preservation of the teeth, which has been practiced in the past almost wholly for mechanical or cosmetic purposes. Preventive measures should begin in childhood, with a view to obtaining proper development of the teeth and oral cavity. The principles underlying various procedures for the prevention and cure of infections of the gums and enveloping membranes of the roots of teeth are fairly well understood and effectively applied by many.

Infections of the dental pulp, pulpless teeth and apical abscesses are theoretically the most dangerous of the various forms of dental foci. They are usually free from symptoms and

hence unsuspected. They are situated in osseous tissues which allow no expansion. They can drain only into the circulation and are exposed to pressure transmitted by the teeth during mastication. They remain active for years, and the bacteria are not encapsulated, as is usually assumed, but are found in areas of active inflammatory reaction where the formation of new blood vessels affords drainage into the circulation.

The bacteriologic study and the animal experiments carried out by me, by Meisser and others working with me, by Price, and especially by Haden, prove that vital teeth free from caries are usually sterile but that practically all pulpless teeth removed from patients are infected, and that, with the organisms, usually streptococci, isolated, the disease causing the patient suffering may often be reproduced in animals. The infection is present whether or not the teeth show rarefaction in the radiogram. Moreover, it does not seem to make much difference whether the root canal had been "properly" filled or not. The idea of focal infection has often been wrongfully condemned because one or more pulpless teeth that showed rarefaction had been removed from a patient without benefit when teeth that showed no rarefaction were thought to be sterile and were left untouched, or when foci elsewhere were not even considered. Again, simple extraction of infected teeth is usually, but not always, sufficient to eliminate infection in the jaw. This seems regularly true if teeth have been rendered pulpless artificially. In the individual case, that method of removing infected teeth should be chosen which assures elimination of the infection, which is least destructive and which is associated with the lowest incidence of constitutional reactions manifested by fever and exacerbation of the systemic condition. Exacerbation following extraction of teeth should be regarded as experimental proof that the infection around the teeth removed has causal relationship and that in all likelihood not all of the infected tissue was eradicated during the operation.

A tooth from which the pulp has been removed or which has died from infection seems to have a lowered resistance to bacterial invasion. The methods generally used in root canal work are certainly not adequate to prevent subsequent infection. The wholesale devitalization of teeth and the filling of root canals, often for trivial reasons, as practiced in the past, should, in the light of our present knowledge, be regarded as veritable experiments on human beings. It is to be hoped that an efficient method may be found that will not only sterilize pulpless teeth and periapical tissues that have become infected, but

will also prevent subsequent infection, especially of the periapical tissues. The fulfillment of the latter requirement seems almost unattainable. Until this has been accomplished, it would seem wiser to remove teeth that have become infected or that require extirpation of the pulp than to retain them and have them become a source of infection later. No one deplores more than I the ruthless extraction of teeth that has been practiced in some instances as a result of the work on focal infection. Vital teeth free from pyorrhea should never be extracted except as it becomes necessary for restorative work. The extraction of pulpless teeth seems to me to be indicated, regardless of the appearance of the radiograms, in cases of serious systemic disease for which no other focus can be found. Good effects are especially prone to follow in cases in which it is possible to reproduce the disease in animals with the bacteria isolated. The results from the use of vaccines prepared from the strain proved to be guilty are also often strikingly favorable. Since the diseases that are commonly the result of focal infection are usually due to streptococci, immunity to which is of short duration, not too much should be expected from the use of specific vaccines or serums. They cannot take the place of removal of a cause, the focus.

The removal of foci of infection, particularly if the focus is situated in tissues that may be readily spared, such as tonsils and teeth, should be practiced in certain instances not only as a curative but also as a preventive measure. General deleterious effects, including lowered resistance to intercurrent infection, as well as specific localization, occurred in dogs in which focal infection had been induced artificially in teeth. This may be regarded as furnishing an experimental basis for the improvement in general health so commonly observed, and for the favorable results obtained in the treatment of diseases such as diabetes, syphilis and pulmonary tuberculosis following the elimination of foci of infection.

A careful consideration of all the facts now available indicates that a sane and comprehensive effort toward the prevention of septic foci and their cure, wherever found, will often result in the prevention and cure of chronic disease, in the alleviation of human suffering in a better preservation of the tissues in old age, in a longer average duration of life, and in increased mental and physical efficiency, and will, through the laws of heredity, make for a sturdier race. Since focal infection is so common in the teeth and surrounding structures, the dental profession may confidently be expected to do its full share in preventive and curative medicine of today and of tomorrow.

FOCAL INFECTION.*

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Focal infection is a localized nidus of pathology in the patient's own body. It is both one of the most recent and one of the most remote conceptions in medicine. It is the lodgment of bacterial colonies in localized areas or organs of the body, where they multiply, incubate, and throw their toxic products into the blood stream, thus producing various acute and chronic diseases.

It has been largely through the efforts of E. C. Rosenow, an eminent pathologist, and later with his disciples and co-workers, Herman C. Bumpus, Jr., and John C. Meisser, that the development of focal pathology has been achieved. Abraham Jacoby and Frank Billings, and many others of equal note have added greatly to this pathology.

These bacteria invade the tissues of the body in such a way as to favor their growth and permit their toxins to injure the tissues. Those most frequently attacked are muscles and nerve tissues in the form of rheumatism and neuritis. The exact manner in which these foci spread their infection to remote parts of the body or produce a general systemic infection is still a matter of discussion. Rosenow has shown that the micro-organisms involved in focal sepsis have an elective affinity for certain tissues and organs, and if from the lesions produced cultures are made and injected into animals, similar lesions in similar organs are reproduced. It is therefore possible, in many cases, to establish a definite relationship between a focus of infection and the disease which is suspected to arise from it.

The tonsils seem to have the most generally recognized portals of entry for systemic infections, and the coincidence between disease of the tonsils and rheumatism, arthritis, etc., led to an investigation of their probable connection and the establishment of the doctrine of focal infection. Jonathan Wright, of New York, in 1906, discussed the way by which the tonsil arrested the entrance of germs into the body and the conditions under which that mechanism broke down. In the same year the celebrated pediatricist, Abraham Jacoby, cited a number of facts in support of toxin absorbing and transmitting power of the tonsils. He also pointed out that the tonsil was not the only pharyngeal route of invasion, but that the lymph apparatus of the pharynx itself played an important part in the process—a view fully sustained by Thomas R. French, in a paper read before the American Laryngological Society in 1920.

It is almost universally accepted that in-

fection often enters through the tonsils and the peritonsillar tissues, and that acute rheumatism, endocarditis and many other forms of streptococcal disease are thus introduced into the system.

The precise anatomical and pathological mechanism by which tonsillar infection takes place is still largely uncertain, but the work of Rosenow, and the later work of the Division of Experimental Bacteriology of the Mayo Foundation, have made it reasonably certain that the micro-organisms involved are certain strains of streptococci, particularly the viridans and the gram negative. It has been amply shown that even in remote infections where the colon bacillus appears to be the predominant bacterial agent, the tonsillar streptococcus is the original cause of the disturbance.

It is a well established fact that even virulent invasions can take place through the tonsillar portals without reactionary inflammatory changes in the tonsillar tissues themselves. A thin layer of epithelium in the interior of the crypts is easily and frequently damaged, affording a ready passage to the lymph channels; therefore it is not uncommon to find very slight tonsillar irritation the forerunner of more or less severe systemic infection. On the other hand the onset of acute rheumatism, endocarditis, etc., is often preceded or accompanied by an attack of acute tonsillitis. Bumpus and Meisser report that: "It is our custom to have tonsillectomy performed in all cases in which the urinary infection may be reasonably believed to be the focal origin. Since we have adopted this procedure a surprisingly large number of apparently negative tonsils has been found to hide deep-seated, virulent infections." Their experience is that of most clinicians and investigators. On superficial examinations the small tonsil appears to be harmless, while the larger one by its size and projection into the throat will often be recommended for removal. This may seem on first impression the proper course to pursue, but Hermon C. Bumpus says that from the viewpoint of focal infection the reverse is probably true. The small tonsil is generally buried deeply in the tissues, and it may be difficult or impossible to demonstrate that it harbors infection, although its buried location makes absorption from its crypts easy. The large tonsil, through its projecting position, has a tendency to drain into the throat, and the exudates and bacteria are swallowed and rendered comparatively harmless.

In two hundred cases of arthritis, reported by Nathan P. Sauffer, in which 66 percent were found to have diseased tonsils, a large number were removed and in cultures made

*Read before the Davie County Medical Society.