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DENTAL SEPSIS IN RELATION TO ANAEMIA, DYSPEPSIA, AND RHEUMATISM

WITH PARTICULAR REFERENCE TO TREATMENT

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I. Historical Introduction

Interest in the problem of dental infection and its relationship to general disease is said to go back to the days of Hippocrates (Kersley, 1938), but the earliest reference of importance is an article by Rush (1818) claiming that a case of arthritis of the hip was cured by the extraction of infected teeth. Black (1918) cited evidence to show that dental infection was considered responsible for infections of the eye as early as 1842. Canton (1880) gave brief reports of cases in which defective and infected teeth were said to have led to dyspepsia, constipation, and even sciatica. He considered the mechanical factor more important than the infective, and claimed great benefit from the use of dentures. Ten years later Garretson (1890) noted the association of chronic periodontitis with "rheumatic and toxical conditions as well as with scurvy and phosphorus poisoning," but he was not inclined to regard the teeth as the primary cause. Miller (1891) collected 149 cases of serious complications of dental infections. These complications were, however, nearly all acute inflammatory conditions. Rheumatism and anaemia do not appear among the recognized complications of dental sepsis at that time, but dyspepsia was sometimes attributed to the swallowing of pus.

William Hunter (1898, 1900, 1904) in a series of articles further emphasized the importance of swallowing pus as a cause of gastritis and "septic anaemia." In later articles (Hunter, 1911) he pointed out that in addition to open and obvious infection, sepsis concealed by crowns and bridges might play a decisive part. A few years later Billings (1916) and Rosenow (1914a, 1914b, 1915, 1916) published a series of articles on dental infection as a cause of systemic disease, and stressed particularly the "closed" apical infection, which only a radiograph could reveal, as being an important cause of chronic toxaemia, rheumatism, nephritis, and many other conditions. The conception of dental sepsis as a major cause of chronic systemic disease really dates from that time. The present common practice of extracting septic teeth in diseases of obscure origin followed directly from this theory.

In the past twenty-five years such a large number of papers have been published on the subject of focal dental infection that it would be impossible to discuss them all in a short article. The following brief summary will review some of the arguments in favour of the theory that dental sepsis can lead to systemic disease, and the main criticisms which have been, and can be, raised against them.

II. Summary of Recent Work

When teeth are infected a variety of organisms may be found in the mouth, but streptococci, especially non-haemolytic varieties, are generally held to be responsible for systemic disease secondary to dental sepsis (Weston Price, 1923; Rhoads and Dick, 1932; Bulleid, 1930). Following extraction of teeth these streptococci may be found in the blood stream (Okell and Elliott, 1935), and possibly manipulation of the teeth or chewing (Ryle, 1938) may lead to the same result. Infective endocarditis, moreover, may follow dental extraction if the heart valves are previously damaged by rheumatism or are congenitally defective. These cases indeed afford the most clear-cut example of focal dental infection leading to systemic disease.

Attempts to produce gastric and arthritic lesions have been made by the experimental injection into animals of streptococci derived from the dental alveoli. Gastric lesions, arthritis, and nephritis (Rosenow, 1916; Weston Price, 1923) have been produced, but such lesions are acute, and either heal rapidly or lead to death. The claim has been made (Rosenow, 1914b) that streptococci may show "elective localization" for some particular parts of the body. Thus streptococci isolated from the teeth of patients with arthritis are said to cause arthritis on injection, while those obtained from patients with peptic ulceration lead to gastric lesions. This work, however, does not seem to have been confirmed in this country (Appleton, 1934). Moreover, streptococci cannot usually be isolated from the joints in rheumatic conditions (Okell, 1937) or from gastric ulcers (Hurst and Stewart, 1929). Some therefore talk of "streptococcal overload" (Bulleid, 1936) or "toxaemia acting as a contributory cause (Broderick, 1936). This is mere conjecture.

We are not in a position to discuss the bacteriology fully. There is a prima facie case at least that infective endocarditis may arise by spread of infection from the teeth to the blood stream. But it does not appear that any strong case can be made for the view that anaemia, peptic ulcer, or the different types of chronic rheumatism are caused by a streptococcal infection arising in the mouth or elsewhere. Indeed, none of Koch's postulates is satisfactorily fulfilled.

Bacteriological evidence being inconclusive, many writers have tried to obtain clinical evidence for the theory. Here all workers have encountered the same difficulties. Before the advent of dental radiology the recognition of dental infection depended entirely on inspection, and attention was therefore largely confined to pyorrhoea and acute alveolar abscess. Subsequently, when it became possible to demonstrate rarefying osteitis about the roots of "dead" or pulpless teeth, these were extensively studied. Haden (1924) and Weston Price (1923) came to the conclusion that this "closed" or latent form of infection was more important than the "open" or obvious dental infection. Recently, however, it has been pointed out that even in "open" cases of pyorrhoea toxic absorption from pocketing may occur, and this, it is held, may then be responsible for systemic disease (Fish, 1937; Fish and Maclean, 1936). According to Rhoads and Dick (1932) even "radiologically negative pulpless teeth" may be important septic foci. The practical conclusion remains. however, that without radiology it is impossible to assess the degree of dental sepsis, and even with its aid estimation is uncertain. This difficulty invalidates much work already published.

Dental sepsis at one time or another has been held to be the cause of anaemia, dyspepsia, and rheumatism. We will discuss these conditions in turn.

Anaemia

Since the introduction of liver therapy for pernicious anaemia and the fuller understanding of haematopoiesis which has followed, dental sepsis has received little attention as an aetiological factor in anaemia. In a recent review (Wilkinson, 1936) dental sepsis is not mentioned at all. It may seem, therefore, that to include anaemias in this discussion is to exhume unnecessarily a buried and forgotten theory. History is, however, instructive. In 1904 Hunter pointed out that in cases of anaemia the mouth was often grossly infected, and he described cases in which treatment of the mouth had led to great improvement in the anaemia. A number of further isolated successes were then recorded. The importance of streptococci in the duodenum was next discussed in relation to achlorhydria (Woodwark and Mackenzie-Wallis, 1912), and the orthodox treatment of pernicious anaemia came to include the eradication of even the smallest septic focus in the mouth (Hurst, 1923). This in practice meant that the patient was rendered edentulous in nearly every case, but he seldom derived any benefit from this procedure. In spite of these depressing results the theory of dental sepsis continued to dominate the treatment of pernicious anaemia, until the advent of treatment with liver (Willcox, 1923). It then sank into oblivion with dramatic rapidity, which suggests that it had little to support it, and that it had merely served as a convenient cloak for ignorance. The danger of lightly assuming that infected teeth are the cause of systemic disease is well illustrated in pernicious anaemia, and the question naturally arises whether the evidence is more convincing in other conditions.

Dyspepsia

A large number of articles have been written to show that dental sepsis is more common among cases of peptic ulceration and carcinoma than among controls. Stead-

man (1923) found a high incidence of dental sepsis in gastric and intestinal carcinoma, though these figures were severely criticized in a leading article (Lancet, 1923) shortly afterwards. In Holland, where the incidence of gastric carcinoma is much higher than in this country, the incidence of dental sepsis is said also to be much higher (Herbert and Bruske, 1936). The series published by Hurst and Stewart (1929) shows that among 187 patients with proven peptic ulceration (positive radiographs) only 16 per cent. had sound teeth. In a control series there were 43 per cent. with "sound teeth." The number of edentulous patients and patients with open sepsis was greater in the "ulcer" than in the control group. In Lossius's (1937) series of 308 cases (half with peptic ulcer and half with "functional" dyspepsia) only 10 per cent. were dentally sound, while in a control series only 25 per cent. were in a "deplorable dental and oral state." The evidence is not very convincing, but it may be that the incidence of dental sepsis is higher among patients with peptic ulceration and gastric carcinoma than among the general population.

The results of dental treatment in cases of peptic ulceration and in "functional" dyspepsia are difficult to assess. Lossius states that of 100 cases having dental treatment 30 per cent, remained symptomless over periods of one to four years, while of 228 without dental treatment only 17 per cent, remained symptomless. These figures can be criticized in many ways, though they probably are the best that can be obtained. Other treatment in the form of diet and alkalis was given to all patients, and, indeed, it would have been unjustifiable to do otherwise. Those patients who consented to dental treatment were probably also the ones who carried out the rest of their treatment most conscientiously. In many long-standing and intractable cases all the teeth had probably already been extracted without benefit before first attending Lossius's clinic. The period of follow-up was not long enough, as relapse may often occur after two. three, or even four years of freedom from symptoms. If the number who relapse be considered, the figures are 70 per cent. and 83 per cent. respectively, and with such a high incidence of recurrence in both groups the relatively slight difference does not seem convincing evidence of the value of dental treatment in this condition.

Rheumatism

Dental infection has probably been more discussed and more radically treated in this group of conditions than in any other. As the aetiology of the rheumatic conditions is not understood, any form of classification must be tentative, but at the same time some subdivision is clearly necessary. The conditions which principally require discussion here are acute or subacute polyarthritis, often referred to as "rheumatoid arthritis"; a chronic type usually mono-articular, referred to as osteo-arthritis; and a non-articular group called fibrositis or muscular rheumatism. Statistics on the incidence of dental infection in such cases vary widely. Moorehead (1916), in America, gives the incidence of apical infections of the teeth as 89 per cent. among seventy patients with arthritis, while it was about 70 per cent. in 150 controls. Irons (1916) gives a figure of 76 per cent. among "arthritic patients" against 44 per cent. in an unselected series of 124 cases. Glover (1923), in this country, estimates the percentage of "clean mouths" in rheumatoid arthritis as 6 to 10, and in the general population as 14 to 20. His paper, unlike many, at least gives some idea of the type of arthritis under consideration, but it does not seem to

afford conclusive evidence that any causal relation between rheumatism and dental infection actually exists.

Undoubtedly the removal of infected teeth is occasionally followed by a marked improvement in an acute or subacute arthritis. Isolated examples of this are found in the literature (Billings, 1916; Haden, 1924; Weston Price, 1923; Tiemann and Schittenhelm, 1934), and are even recorded by those who consider the importance of dental infection in arthritis to be grossly exaggerated (Bach, 1935). These isolated examples are of doubtful significance, as the course of the disease is always variable and other forms of treatment, especially rest and heat, are generally and very properly used simultaneously. satisfactory comparison has yet been made between cases treated without eradication of dental sepsis and those in which eradication has been practised. Indeed, as is mentioned in a later section, it is almost impossible in practice to collect such a series. Pemberton's (1929) series, which is an attempt to elucidate this point, includes many varieties of the rheumatic diseases. The individual groups are therefore small, but they certainly do not suggest that the eradication of septic foci improves the results of treatment to any great extent.

It is now fairly widely admitted that cure of rheumatic conditions following dental extraction is the exception rather than the rule (Bennett, 1931; Broderick, 1936), and Kersley (1938), in a review of dental infection in rheumatism, admits that the results are often disappointing even in the rheumatoid group, which he considers the most definitely infective. It is argued that in advanced cases cure could not be expected, as irreversible changes have taken place in the joints, and that in some cases other septic foci are present and keep up the infection. Both these statements may be true of particular cases, but they do not affect the main conclusion that eradication of dental sepsis is only occasionally of value in the treatment of rheumatic diseases.

Summary.—Dental infection has been claimed as a causal factor in anaemias, dyspepsias, and rheumatic diseases. The evidence in each case has been derived partly from experimental bacteriology, partly from a statistical study of the incidence of the two conditions, and partly from the results of treatment. All three lines of evidence have been subjected to serious criticism. The bacteriology does not fulfil Koch's postulates. The high incidence of dental infection in these conditions, if indeed it really is significant statistically, does not necessarily indicate a causal relation. The results of treatment are distinctly equivocal.

III. Clinical Observations

The relation, if any, between dental sepsis and dyspepsia or rheumatism is difficult to establish. The obvious way to investigate this problem would be to collect 100 cases of dyspepsia and 100 cases of rheumatism, investigate the dental conditions, and subject half the cases with dental sepsis in each group to dental treatment and let the other half remain untreated as controls. But after a year's trial we abandoned this method of investigation as being impracticable, for the following reasons:

- 1. It is difficult to assess or classify in any satisfactory way the various types of rheumatism and dyspepsia.
- 2. The variation in the degree of dental sepsis present in these cases is great, and it is difficult to assess this with any degree of accuracy.
- 3. There is a tendency in dyspepsia and rheumatism to spontaneous remissions, often extending over long periods,

- 4. Treatment such as the use of alkalis in dyspepsia, and empirical methods in rheumatism, can hardly be withheld, or, if withheld, the patient seeks and obtains treatment elsewhere.
- 5. Many patients refuse dental treatment, or come to hospital for the first time having already had their dental condition radically treated elsewhere.

It is these difficulties which have nullified all attempts to prove the relation between dental disease and dyspepsia or rheumatism, and which account for the present unsatisfactory position of the theory of focal sepsis.

During the course of a preliminary investigation along these lines, however, we were impressed by the large number of patients attending a general out-patient clinic who were already edentulous. We therefore decided to ascertain from every edentulous patient who came to the clinic for any reason:

- (a) When he had had all his teeth out;
- (b) Why he had had all his teeth out—that is, whether for purely dental reasons, or on account of rheumatism or dyspepsia; and
- (c) If on account of rheumatism or dyspepsia, whether these symptoms had been ameliorated, had remained the same, or had become aggravated.

These patients were all attending a general out-patient clinic which was not restricted to any particular type of disease. They therefore represented a relatively unselected group. As, however, a large clinic for the investigation and treatment of rheumatic conditions coexists in the same hospital, the proportion of cases of rheumatism attending our department was much less than would otherwise have been the case.

Admittedly this method of approach must give a onesided picture of the situation. We have seen the failures—the cases in which dyspepsia or rheumatism has followed or has not been relieved by radical dental treatment. Cases in which removal of the teeth has restored the health, or cured rheumatism or dyspepsia, will not have come our way as a rule. We maintain, however, that if the failures are numerous, then grave doubt is thrown on the wisdom of applying the theory of focal sepsis as a guide for the treatment of these conditions.

The result of this investigation of 234 edentulous patients may be stated in the following way:

Group A—Teeth extracted for purely dental reasons			 126 (54%)	
Group B-Dyspepsia present before extraction			 76 (32%)	
Group C-Rheumatism present before extraction			 13 (6%)	
Group D-No satisfactory history obtainable			 19 (8%)	

We have subdivided the cases of dyspepsia into two types—the peptic ulcer type and the functional type. We have included under the heading "dyspepsia of peptic ulcer type" those cases in which pain was a prominent feature, had a definite relation to meals, and was relieved by alkaline powders. In many of these cases the diagnosis of ulcer was confirmed by radiography, but we have not hesitated to include under this type those cases in which the radiograph was negative, provided the history was typical in these respects, and also cases with haematemesis. (Presumably in these patients the ulcer is too small to be visible, or the local gastritis is still in the preulcerative stage.) We have included under the heading of "dyspepsia of a functional type" those cases in which pain was not a prominent feature and the main symptoms were discomfort, nausea, fullness after meals, and flatulence. These cases are often labelled chronic gastritis, nervous dyspepsia, chronic cholecystitis, or visceroptosis, according to the fashion of the day and the views of the physician. More accurate diagnosis is probably impos2 (3%)

70 (93%)

sible. For the patients complaining of rheumatic symptoms no subdivision has been attempted because, as has been explained above, they were too few to give any satisfactory indication.

GROUP A.—Cases in which all the Teeth were Extracted for Purely Dental Reasons, and No Symptoms of Rheumatism or Dyspensia had been noticed Before that Time

or Dyspepsia n	aa v	een n	onced	і веј	ore i	nai	1 ime	
Cases developing dysper	tic sy	mptom	s after	extra	ction	of a	ll teeth	39 (31%)
Developed dyspeptic	symp	toms at	once :					
Of a functional						8		
Of peptic ulcer t	ype					1		
Haematemesis						1		
						10	(8%)	
Developed dyspeptic	symp	toms 2	or mo	re year	s late	r:		
Of a functional Of peptic ulcer	type	. ·.	••	٠	• •	13		
Or peptic dicer	type.	-6:		• •	• •	10		
Developed carci	noma	or ston	iacni	• •	• •	0		
3 · *						29 (23%)	

	-> (-> /	
Cases developing rheumatic symptoms		 19 (15%)
Cases not developing rheumatic or dyspeptic symptoms		 68 (54%)
· · · · · · · · · · · · · · · · · · ·		
the state of the s	•	126

* Seven of these confirmed radiologically or at operation. † Five of these confirmed radiologically or at operation. GROUP B.—Cases in which Dyspeptic Symptoms were Present

Before all the Teeth were Extracted (76 Cases) Permanently relieved . 6 (7%) Organic dyspepsia (duodenal ulcer) Functional dyspepsia Not permanently relieved: 27 (36%) 6 4 17 • • Unchanged ... Functional type ... Aggravated ... Temporarily improved No change ... 41 (54%) 9

* Nineteen of these were confirmed radiologically or at operation. † Both of these confirmed at operation.

Total number of cases not relieved . .

Developed carcinomat

GROUP C.—Cases in which Rheumatic Symptoms were Present Before all the Teeth were Extracted (13 Cases) Symptoms relieved mptoms relieved ...

As the foregoing method did not give any indication of the relation of dental sepsis to anaemia, we took the opportunity to study the dental condition of fifty-two patients attending a special haematology clinic. We are indebted to Dr. Donald Hunter for leave to investigate these patients in this way. The results may be summarized as follows:

	Macrocytic (Pernicious) Anaemia	Microcytic (Hypochromic) Anaemia
Edentulous for many years before onset of symptoms of anaemia	13	10
All remaining teeth removed when anaemia first diagnosed	. 4	1
Patients with obviously infected teeth	9	10
Patients with apparently sound teeth		5
Totals	26	26

In all these cases the condition of the blood had been fully investigated and treated successfully, and the diagnosis was not in doubt. The dental condition also could not be doubted, except in those which we have described as having "apparently sound teeth." Here radiology might have revealed infection which was not obvious clinically.

From the practical point of view two salient features emerge even from a small series such as this. The removal of dental sepsis by extraction will not prevent the onset of macrocytic or microcytic anaemia, and the presence of dental sepsis will not prevent a satisfactory response to treatment with liver preparations or iron as the case may be,

Discussion

The theory of focal sepsis has now been under discussion for over twenty years, and sepsis in relation to the teeth has been used to explain numerous diseases of obscure aetiology. In Germany and France the theory has not been generally accepted, but in this country, and to a greater extent in the United States of America, it is still widely held, and eradication of septic foci, if present, is usually part of the routine treatment of rheumatism and dyspepsia.

Our experience, however, in an out-patient clinic of a general hospital has led us to question the wisdom of the uncritical adoption of this practice. Frequently we have come across patients who have consulted a doctor on account of rheumatism, dyspepsia, or vague ill-health, and have been sent to a dental surgeon for an opinion on teeth which looked unhealthy. In these patients the doctor's opinion has been confirmed, and the dental sepsis has been found to be more extensive than was at first supposed. Even so, in many of them some teeth were probably in fair condition and might have been retained. But a partial denture would then have been necessary, and this would almost certainly have had to be replaced by complete dentures in a few years. They consequently have preferred, for reasons of economy, to have all the teeth extracted together. Few insured persons could afford the expense of temporary dentures for immediate use, and these patients had therefore to wait for a considerable time until their gums had hardened and retracted sufficiently to have permanent dentures fitted. Under the National Health Insurance Act a minimum period of three months must elapse between extraction and the fitting of dentures; but in practice this period was seldom less than six months in these patients, and meanwhile they had had to eat as best they could without any natural or artificial teeth. Dyspepsia developed for the first time or was aggravated soon after the extraction of septic teeth in so many of these cases that we have come to the conclusion that the mechanical factor introduced by the lack of natural teeth is at least as important as, possibly even more important than, the toxic factor in the pathogenesis of dyspepsia which is supposed to be associated with chronic dental sepsis.

The view is widely held that dental sepsis is a common cause of indigestion. There is, however, so far as we can see, no convincing evidence of this. In our experience indigestion is often started or aggravated by the removal of septic teeth. We have come to the conclusion that in the treatment of dyspepsia, particularly in elderly subjects, the removal of teeth must only be advocated with caution, because, even if the primary cause of the dyspepsia can really be removed in this way, a serious mechanical factor is introduced, and the patient's condition is often not only not improved but may actually be aggravated. There are various reasons for this. The patient may be left without any teeth for several months. When dentures are fitted they are by no means always satisfactory. They may fulfil their aesthetic functions but be useless for the purpose of mastication. We have come across a number of patients who take their dentures out to eat their meals. In other cases dentures are more satisfactory, but they may yet be a poor and inefficient substitute for natural teeth. There may, of course, be instances in which dyspepsia is actually cured by removal of septic teeth. As we have already explained, these cases would not come our way, but we are inclined to think that their improvement may be attributed not so much to the removal of the septic factor as to the replacement of inefficient natural teeth by dentures which are more efficient mechanically. In the prophylaxis of dyspepsia, therefore, a healthy mouth is of great value in order that sound natural teeth may be conserved as completely and as long as possible. When they are lost immediate and faultless prosthetic dentistry is essential.

The relation between dental sepsis and rheumatism is even more uncertain. We do not wish to underrate the importance of a healthy mouth in the maintenance of the general health, or the efforts of dental surgeons to accomplish this ideal. The fact remains, however, that there is no convincing evidence that dental sepsis is a cause of rheumatism. Our own series is admittedly too small to give any satisfactory indication, but it seems probable that all forms of rheumatism can arise for the first time in an edentulous patient and that, apart from the mechanical factor, which does not arise, the position is similar in rheumatic conditions and in dyspepsias. Furthermore, gross dental infection is apparently compatible with good general health. It is suggested, therefore, that teeth should be treated on their merits in each case, regardless of what rheumatic or dyspeptic symptoms may also be present. Indiscriminate removal should not be advocated on the theory that it will influence the course of the disease.

Summary

An inquiry has been made into the after-histories of 234 out-patients in whom all the teeth had been removed for various reasons.

Seventy-six of these patients had previously suffered from dyspepsia, and the teeth had been removed on the theory that dental sepsis was responsible for their condition. Six had been benefited. Thirteen had previously suffered from rheumatic symptoms, and extraction of septic teeth appeared to have had a beneficial effect in five cases.

In 126 cases the teeth had all been extracted for purely dental reasons. Thirty-nine of these patients developed symptoms of dyspepsia, and nineteen developed symptoms of rheumatism.

The widely accepted relation between dental sepsis and dyspepsia and rheumatism is questioned. The mechanical factor, due to inadequate teeth, would appear to be more important than the septic factor in the pathogenesis of dyspepsia.

A healthy mouth is valuable largely because it leads to conservation of the teeth. When extraction cannot be avoided, early, adequate, and efficient prosthetic dentistry is essential in the prophylaxis of all types of dyspepsia.

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POTASSIUM TELLURITE IN THE DIAGNOSIS OF DIPHTHERIA

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An annotation in the British Medical Journal of December 3, 1938 (p. 1152), drew attention to a paper published by Dr. Manzullo of Buenos Aires on the possibility of bedside diagnosis of cases of diphtheria with pharyngeal exudate. Reference to this paper (Manzullo, 1938) showed the following points or claims:

- 1. A 2 per cent. solution was made of potassium tellurite in distilled water. Care was taken to avoid heating above a temperature of 40° C. in effecting the solution. The solution was said to lose its efficiency after a month.
- 2. The solution was applied to various throat exudates by means of a swab, care being taken to avoid touching the tongue in so doing.
- 3. From five to ten minutes afterwards the throat was examined, and in some cases a definite darkening of the exudate was observed.
- 4. This procedure was applied to a series of seventy-five cases showing pharyngeal exudate. Of these cases forty were bacteriologically diphtheria, and darkening was observed in thirty-seven of them. In the thirty-five cases not due to diphtheria no darkening was seen at all.

These figures suggested that diagnosis on the presence or absence of diphtheria in cases with a pharyngeal exudate could be made simply and easily at the bedside with an accuracy of 96 per cent. With a view to corroborating this work a similar investigation was started at the Leicester City Isolation Hospital, and the results obtained are described and discussed below.

The Technique used in the Present Investigation

The solution as described was effected with little difficulty. Experiments on the "keeping power" of the solution confirmed Dr. Manzullo's findings that it was unwise to use a solution more than four weeks old. The darkening when it occurred was obvious. One case of