A British Medical Association Lecture ON "PERNICIOUS ANAEMIA" AND "SEPTIC ANAEMIA."

WITH NEW OBSERVATIONS ON THE DISTINCTIVE SORE TONGUE,
SEASONAL INCIDENCE AND POWERS OF RECOVERY OF
"PERNICIOUS ANAEMIA," NOW TERMED
"GLOSSITIC ANAEMIA."

BY

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INTRODUCTORY.

THE subject of anaemias, selected by the Council of the British Medical Association for my address to you to-day, has been one of peculiar interest to me for over thirty-five years. Incoming back to it now after a break in that interest occasioned by the war, I have put to myself the question, What has been the practical outcome of it all? And I have thought that I might best help it if I endeavoured to-day to consider before you what new light, if any, this prolonged study has thrown either on the nature, the diagnosis, or the treatment of those forms of anaemias that are obscure and give trouble both in diagnosis and treatment—forms best designated as severe to distinguish them from others that are simple in their character.

In my remarks to you to-day I shall draw on my experiences, and illustrate them by the specimens and plates shown to you, without adhering to the final form which I have sketched out and now give to this address. The former is easy to me, while the latter, owing to the abundance of material at my disposal, is difficult. And yet I feel a great desire to put together in the form of one address the salient facts of that experience, in the hope that by so doing I may give you something that may help you in your outlook and practice in connexion with blood diseases generally and severe anaemias in particular.

The infective and clinical features of severe anaemias go deeper into their nature and help far more in diagnosis and treatment than the various blood criteria so much before our notice in dealing with anaemias. Such sums up in one sentence the most important outcome of my studies, and may well be taken as the text of my address to you to-day.

I am not going into the matter of these blood changes with you to-day. Indeed, in all my various studies and writings I have kept them in the background. I have had a great purpose in doing so. As detailed in the formidable list of percentages familiar to us in blood reports they make a deep impression on the eye and on the mind—that surely here, if anywhere, the full facts regarding anaemias must be found. Unfortunately this is not the case. For they have one great drawback—namely, they always fail precisely in the borderline group of cases, in which the clinical observer most needs their help. Secondly, they always fail whenever the anaemia is moderate in degree, and when it is particularly necessary to be sure of the character of the anaemia with which we have to deal if successful measures are to be taken in time to arrest its progress.

Infective Criteria.

On the other hand, the outcome of the study of the infective and clinical features presented by cases of severe anaemia has yielded me the following information, which I summarize in five paragraphs, and shall afterwards amplify in the course of my address:

1. Two forms of severe anaemia are to be recognized. The one is the great haemolytic disease, *sui generis*, termed idiopathic or pernicious anaemia. The other is a very common anaemic condition—non-haemolytic in its nature—which I have differentiated and term septic anaemia (1900). It is these two classes of severe anaemia with regard to which I propose to-day to describe the final outcome of my studies.

2. That outcome reveals that the patient who presents the picture of desperate anaemia—termed pernicious, as it was presented and as it is still presented when first seen—is really in the grip of both the above forms of anaemia, each of them capable of killing him, and the two combined absolutely mortal. The chief one that gives his illness its main characters and clinical features and course is the haemolytic disease termed pernicious anaemia; the other complicating one is the above-mentioned non-haemolytic septic anaemia.

* Delivered before the Devon and West Somerset Branch at Taunton, November 15th, 1921.

3. The practical outcome of this recognition and differentiation which I propose to describe to you to-day is that the two anaemias can be torn apart by removing completely the septic anaemia and its causes from the pernicious anaemia patient. On doing this the great haemolytic disease which remains shows itself for the first time in its history in its true uncomplicated characters and course; and these prove to be much milder in severity and with a much better prognosis than were ever formerly presented.

4. The further outcome of these studies has been to reveal certain simple and easily recognizable clinical diagnostic features which enable the haemolytic disease "pernicious anaemia" to be recognized in its very earliest stages—even within a few weeks of its first contraction, long before the existence of this anaemia has been ever dreamt of, and on an average about two years before it generally comes under treatment.

5. The infective and clinical features here referred to, that help so much in diagnosis and treatment of both classes of anaemia, are connected with observations, not on the blood, but of lesions connected with the mouth. These lesions are combined in the case of the pernicious anaemia patient, but are perfectly distinct from one another, and have a totally different pathological and etiological significance.

The infective lesions connected with, and diagnostic of, the haemolytic disease "pernicious anaemia" are those connected with, and manifested by, the peculiar sore tongue which this disease presents as one of its earliest features. The lesions concerned with the "septic anaemia" are septic lesions connected with chronic and overlooked dental and nasal sepsis, especially the former, to which I have given the name "oral sepsis."

The foregoing being a brief summary of the general outcome of my studies, I now pass on to consider some of the chief facts in the following three sections of my address; Part I: Pernicious anaemia. Part II: Septic anaemia, as an independent anaemia, and as an intense complication of pernicious anaemia. Part III: Great powers of recovery of pernicious anaemia on removal of the sepsis and septic anaemia associated with it.

I.—PERNICIOUS ANAEMIA.

Sore Tongue as the Earliest and Chief Diagnostic Feature of Pernicious Anaemia.

The particular lesion which more than any other I find to be most distinctive of the haemolytic disease "pernicious anaemia" is the presence or history of a peculiar form of "sore tongue" in a patient suffering from an anaemia. Such a history, associated with the clinical features of increased blood destruction (haemolysis), is, in my observations of the past thirty years, since I first described it in the first case I ever studied (1890), the most important infective and diagnostic feature of this great haemolytic disease. So much is this the case that the name which would, in my judgement, most clearly connote this disease, help in its early recognition and subsequent control, and at the same time get rid of the brutal, ill-omened, prognostic, and confusing name of pernicious, would be the title "Glossitic haemolytic anaemia," or, more shortly, "Glossitic anaemia." After many years of perplexing consideration given to the matter, it is that name I now give this disease, and by which I shall henceforth refer to it. I do so in the hope that I may thereby free future observers and future sufferers from this disease from some of the difficulties which for thirty years and more I have experienced in connexion with the name "pernicious"—the worst name ever given in medicine, and a cause of confusion not associated with any other disease in medicine.

The name "glossitic" which I now give it will at least make clear the exact identity of the haemolytic disease, with which my work for thirty years has been concerned—the disease which alone I have ever had in view under the name "pernicious anaemia," or the more distinctive name of idiopathic anaemia of Addison, or the historical name I gave it in my work in 1910 of Addisonian anaemia, or the latest name given to it in an important Continental work in Holland of Addison-Hunterian anaemia.

The great haemolytic disease to which I thus give the name of glossitic anaemia is the disease referred to throughout its history by the following names:

- "Anaemia in its most idiopathic form" (Combe, 1822).
- "Idiopathic anaemia" (Addison, 1855).
- "Progressive pernicious anaemia" (Swiss and German and other observers, 1870-88).
- "Idiopathic pernicious anaemia" (Pye-Smith, 1878).
- "Pernicious anaemia" (all observers).
- "Idiopathic haemolytic anaemia" (Hunter, 1890).
- "Addisonian anaemia" (Hunter, 1910).
- "Addison-Hunterian anaemia" (two chief Dutch writers, 1921).
- Idiopathic "Glossitic anaemia" (Hunter, 1921).

In bringing to an end my long series of studies on this disease and giving it now this final name, may I note that by an interesting coincidence the disease this year celebrates the centenary of its first case recorded in any language—namely, that recorded by Combe of Edinburgh in 1822.

May I note further that the very first words he applied to the disease were: "A very peculiar disease, which will doubtless be viewed in different lights and receive different appellations. If any train of symptoms may be allowed to constitute anaemia a generic disease, the following may be considered an example of it in its most idiopathic form."

May I add, further, the final opinion of the oldest observer who had followed its story for a period of nearly sixty years—from its earliest beginnings in English medicine in the late "forties" of the past century to the final termination of my own work upon it in 1903. The observer referred to was Professor Sir William Gairdner of Glasgow (1903), who said, writing a year or two before his death:

"My earliest acquaintance with the disease dates from the late 'forties,' when I reviewed the first paper in which Addison introduced his idiopathic anaemia idea. All I have seen makes generally for your view of the case. I wish I had taken note of the glossitic phenomena you describe, but I am afraid I am among the number of those who have passed over very much within my view. If you can make that point (the glossitis) clear as being of the frequency you describe, you will have won your case against all gainsayers."

In introducing this name, may I, to save time, anticipate the criticism which I know from past experience of everything connected with the name "pernicious" will assuredly be raised. That criticism is that I have described a "new form" of pernicious anaemia, thereby only making confusion worse confounded. To anticipate this may I repeat that, apart from the disease to which I now give the name of "glossitic anaemia," I have never seen a case of "pernicious anaemia" in my life, or a case of "idiopathic anaemia of Addison," or a case of "Addisonian anaemia," or a case of "Addison-Hunterian anaemia."

What I have done is to obtain the great haemolytic disease in a pure form such as rarely, if ever, previously existed; to find that this disease when freed from sepsis has milder characters and a more benign and better course than it ever before had, and that it deserves some name that will help in its diagnosis and treatment, instead of the name "pernicious," which does neither.

May I also anticipate another kind of criticism which it may at once receive. It was one I heard recently from a student. He had evidently been taught to attach no importance to it, because, as he said, a similar sore tongue could also be found in sprue, scarlet fever, and leucoplakia! Sprue, a disease of which most people have never seen a case; leucoplakia, a condition which is of no vital importance to anyone; and scarlet fever, of which I have seen many thousands of cases, and with whose tongue conditions, it may be presumed, I am well acquainted. The sore tongue to which I attach importance is that found in combination with the twenty-one characteristic clinical features of the disease I term glossitic anaemia.

Sore Tongue Features in Ten Cases.

The sore-tongue lesions I refer to are those I described for the first time in the first case of the disease I ever studied (1890). Their histological characters are illustrated in my work on *Severest Anaemias* (1910), in plates which I now show you. Their constancy is such that I have seen them in every case—150 or more—of which I have full records. Their characters when marked are shown in the coloured plate from the last case under my observation. Their relation to the disease from its origin onwards may be illustrated by the following cases selected almost at random from my records.

CASE I. (*The Original Case, 1889.*)

Illness dated from the autumn of 1887. While on holiday in the country he was exposed for a time to unhealthy sanitary conditions—drain smells. He suffered at the time from sore tongue and sore throat, and never afterwards regained his health.

1887. He continued to suffer at times from an inflamed tongue—red spots on the tongue.

1888 (June). His tongue troubled him very much, tenderness on eating, extending down the throat into his stomach. Tongue extremely flabby, indented by the teeth, presenting a red fiery appearance, with scattered patches of a more inflamed character. Portions of the mucosa being smooth as if devoid of papillae. The redness extended to anterior pillar of fauces.

May, 1889. Tongue much the same as before, not quite so raw; along edges there are patches of more fiery redness. Some of these under tip of tongue show small inflamed vesicles full of serum. (Death took place in May, 1889.)

CASE XII (1901).

About September, 1900, very bad inflamed tongue, deep red. Swelled so that he could hardly get it out of his mouth, and had to take everything cold—anything warm gave him pain. Tongue always more or less tender for some years before—always on the same spot, the right side; with sometimes little vesicles. They came and went, but were never severe till September, 1900, when the attack lasted six weeks. Has not been troubled with it much till now (May, 1901), when it became sore all over and is still sore. It is now smooth and glazed. (Death, 1901.)

(Illustrations of this tongue in *Severest Anaemias* (1910), Plate 2, Fig. 4; Plate 5, Figs. 9 and 10. The changes were extreme in character, nearly all the muscle substance being destroyed, and the epithelial covering reduced to a mere line of cells.)

CASE XV (1901).

A gentleman, an eminent member of the profession, living retired in a large old country house with sporting estate attached. He was fond of gardening. In the autumn of 1900 he spent much time in watering his roses with sewage obtained from an old cesspool, the stench of which was very bad. His tongue became very sore, and at the same time he began to feel very weak and tired at the end of the day. He had formed a small sitting-room from a former gun-room, with which an old lavatory was connected. He used to sit, feeling very wearied, by the fire in this room, between the fire and the lavatory. He then found that there was an old cesspool under his lavatory floor, so that, unknowing, he had again exposed himself to very marked drain infection. He became very ill and anaemic during the autumn (stage of invasion). He had all the features of pernicious anaemia the following spring when I saw him, accompanied by the recurrent sore tongue. He made a remarkably good recovery three months after I saw him, and enjoyed excellent and robust health over a period of eight years, when he died.

He wrote me that he still from time to time had feelings of intense illness, which gave him concern, and a feeling that he still had his old disease on him. I saw him only once, some six years later, in robust health. His tongue was beefy red and very characteristic. He died two or three years later, but I never got any further details.

CASE XIX (1901).

Mouth becomes sore every three or four weeks with what appear to be little "canker spots" on sides; tongue swells and cracks. This lasts about a week, then goes off for a time.

January, 1902. Tongue much better, sores on sides healed, but surface shows a sodden appearance.

February. Patches on side of tongue returning.

March. Tongue better and clean. (Death. Illustrations of tongue, op. cit., Plate 2, Fig. 3.)

CASE XX (1901).

Ill health began in 1898 when she went to stay with friends and slept in an insanitary room for a month. On returning home complained of a sore tongue (incubation period of disease, three to four weeks). It was swollen and raw, so that she could not bear to touch it, a number of ulcers—eight on one side alone—extending all round edges of the tongue, inside the cheeks, and on the throat. She has had this condition off and on ever since about every two or three weeks. Tongue now soft, with angry red patches on sides and tip; at other parts shows atrophy. At two parts, small white patches, like sodden blisters, very tender. Tongue at times swells up almost to teeth.

February, 1902. Tongue very clean.

March, 1902. Three red spots on tongue at tip. On left edge two yellow vesicles about size of a barley seed. Later on improvement and no redness.

CASE XXV (1902).

For last two years "she has always had a sore tongue, so that she could not take wine without a feeling of scalding as far as the stomach." It comes and goes; no vesicles, but little cracks appear on edges and on dorsum. Tongue has now a singularly inflamed look, with cracks all over the edges; great tenderness.

CASE XXVIII (1903).

Tongue became sore about three months ago (September); soreness seems to go right through to back passage. It appears perfectly well for a time, then a relapse occurs once in two to three weeks. It has now a smooth and fissured appearance.

CASE XXXIV (1905).

Ill health began some four years ago (1901), when he had a bad attack of anaemia. Tongue has been sore off and on since 1901. Always noted at the times he is ill. Then the pain goes down to pit of stomach, causing retching and indigestion; then he gets so weak he has to go to bed.

CASE XLIV (1907).

Good health till spring of 1903, when she came in contact with a very foul drain. Tongue at this time began to be sore and red, varying in intensity and distribution; and this has continued up to present time with periods of intermission.

CASE XLVII (1907).

Since 1905 tongue has been very sore—very beefy-looking. Sometimes blood raw. Comes and goes every few weeks. Soreness extends down into stomach, with severe diarrhoea.

1908. Tongue remarkable—bright, fiery red, with cracks on sides and bright red papillae all over.

September. Run down in health and had a bad tongue. Tongue gets inflamed at tip every three weeks, accompanied by some discomfort in stomach and lower down, as if he were inflamed all the way down.

Summary.

I have found a history, similar to the preceding, in all cases I have seen.

It may be summed up as a sudden onset, with a seasonal time of onset (July to September), marked by periodic "sore tongue," periodic "sore stomach," periodic "sore bowel," followed by periodic sore haemolysis, periodic sore anaemia.

The first three features occur singly or combined, varying in intensity at different times; sometimes quiescent, at other times active. This periodicity is very marked in the tongue lesions. At times this looks quite normal; but at other times, generally at intervals of two to three weeks, it becomes tender, and shows patches of redness, or vesicles; or it may become extremely inflamed, looking like raw beef. When the patient is extremely anaemic these tongue lesions are least obvious, since the patient has not sufficient blood in his body to cause redness or inflammation; and in some cases they may be quite absent or quiescent for months at a time.

They are therefore often best seen when the patient is comparatively well or in the stage of recovery. Their recurrence from time to time during the stage of recovery is a most valuable guide in the treatment of the case, since it denotes renewed activity of the disease at different times. These recurrences are always accompanied by evidences of haemolysis—for example, lemon colour, high colour of urine, and some fall in the number of red cells—as observed over a period of fifteen years in a case under my care, which I shall later refer to.

I show you the actual changes in the tongue (and stomach and intestine) as represented in plates in my work, *Severest Anaemias* (1910). The intrahepatic changes of catarrh of the smaller bile ducts associated with the jaundice (haemolytic) occasionally presented by the disease I have also been able to study in a case which died in the acute stage.

Clinical Features and Course of the Haemolytic Disease "Glossitic Anaemia," ushered in by the above Symptoms of Recurrent Sore Tongue.

The disease thus ushered in is the anaemia termed "pernicious anaemia." Apart from the disease marked by the sore tongue above described, I have never seen a case of pernicious anaemia in my life. As regards the individuality and identity of this disease, I draw special attention to two great outstanding etiological characters distinguishing it from all other anaemias.

Individuality and Identity of this Disease.—The first is its most peculiar sex and age incidence in the 150 cases—no fewer than 71 per cent. of the cases being in men, in whom all other anaemias are least common; and 85 per cent. over the age of 40, the age at which all other anaemias are least common. This feature is a hard statistical one, which can be expressed in actual figures as above stated. The haemolytic and glossitic features which, from 1890 onwards, I have described in connexion with this disease I have now called glossitic anaemia, have lifted the identity of this anaemic disease far above the level at which it stood thirty years ago under the title of "pernicious anaemia." The sex and age incidence originally given for the anaemia called by this name (in 1871) was 20 per cent. in the male sex (as compared with my 71 per cent.); and 16 per cent. above the age of 40 (as compared with my 85 per cent.): obviously a totally different class of cases. Nevertheless, in spite of this extraordinary difference, the name I have to give the unique type of disease which forms my group of cases is the same name "pernicious" as that given to a totally different class of case. Hence my resolve now—after thirty years of difficulties connected with the above fact—to give this great haemolytic disease a name that will accurately connote its identity as I find it, and also incidentally connote the disease to which all my work on this disease refers.

The second great outstanding feature of this disease is the last one I described in connexion with it—in 1913. This is the extraordinarily marked seasonal character of its onset and of its periodic relapses—namely, July to September for its onset, and approximately the same months, July to September, for its relapses. I know nothing in connexion with any chronic disease so remarkable or so constant. It places this disease within the category of specific infective diseases in such a striking way that this character of it can be no longer in doubt. No other anaemia known to me has such a character. It is notably absent in the anaemic condition which, when severe, most closely resembles it, and is most frequently mistaken for it—the anaemia which I have differentiated and term "septic anaemia."

All my cases show the same characters and course as the original one. But many show certain other features to which I draw special attention. The first of these is the occurrence of fever as one of the first features in the onset of the disease—fever of obscure nature, generally termed "influenzal" by the patient. This feature is quite a common one. Its chief character is that it is followed by such a surprising degree of weakness and by the lemon colour which denotes the haemolysis of the disease.

Another feature shown in other cases is one of great importance—the surprising degree of anaemia which accompanies this first attack, down to 40 per cent., a fact of importance since it is very seldom that the blood is examined at this period. The same applies to the second attack, which is often also passed through without the question of a severe anaemia having been raised; and yet the blood may be as low as 23 per cent. The recovery from this attack is not so rapid or complete as after the first attack, the blood only rising to 50 or 60 per cent. as compared with 80 to 90 in the first attack.

It is generally only when the third attack occurs that the anaemia becomes so marked as to be a matter of real concern. The question of it being "pernicious" is then raised often for the first time—that is to say, two years after the original attack. It is quite astonishing, indeed, to see from one's reports how often the patient's statement begins that his "illness began about two years ago." It is this important hiatus in the observation and possible control of the disease that can now be bridged over by the diagnostic feature of the sore tongue which I have described. For the patient can often recall, even to within a month, the exact date at which he first began to be troubled with a "sore tongue," and that occurrence marks approximately the first period of onset of the disease.

Lastly, a constant feature is the existence of nervous features in slighter or severer degree in all cases of the disease—visceral pains (in tongue, stomach, or intestine), peripheral, cerebral and mental.

II.—SEPTIC ANAEMIA:

- (a) AS AN INDEPENDENT ANAEMIA;
- (b) AS A COMPLICATION OF PERNICIOUS ANAEMIA.

Interesting and informing as the foregoing facts may be regarding the great haemolytic disease, an even greater interest and practical importance attaches to the second outcome of my studies regarding anaemias. That outcome is the complete differentiation of another form of anaemia which I have termed septic anaemia; and the discovery of the great part it plays not only as an anaemia existing by itself, but even more as a frequent accompaniment and complication of other forms of anaemia, and indeed of other diseases.

Its discovery arose out of my studies (in 1900) regarding the presence of the common septic conditions I termed oral sepsis as an intense complication—not the *causa causans* (pace many erroneous statements)—of the great haemolytic disease pernicious anaemia marked by sore tongue, as I have described in the previous section. I find, namely, that this oral sepsis itself can and often does cause a form of anaemia quite different from the haemolytic anaemia of the sore tongue disease. The anaemia so caused is not an anaemia *stricto generis* as the former is; it is an anaemic condition produced by long-standing sepsis—chiefly streptococcal—such as accompanies dental disease, or may be found from time to time in adjacent parts, especially the antrum and nasal air sinuses.

This septic anaemia is, in my experience, the commonest form of all anaemias. It varies much in degree, often mild, but at times very severe, simulating and approaching even that of the sore tongue, haemolytic anaemia—for example, down to 20 per cent. of red cells. But it differs totally in its pathology from the above-mentioned glossitic (or pernicious) anaemia in being non-haemolytic, and in owing its character to deficient blood formation, just as much as the haemolytic anaemia owes its character to excessive blood destruction. The cause of it in nine-tenths of cases is, as I have just stated, unrecognized and very common sepsis, connected with bad teeth and periodontal disease (pyorrhoea)—"oral sepsis"; in other cases it is overlooked sepsis in the antrum and nasal sinuses.

But, as I have stated, the intense clinical interest of this anaemia is that it may not only exist alone. Far more frequently it exists along with and complicates other anaemias in which similar conditions of oral sepsis are present, and herein lies part of the great importance of oral sepsis in connexion with the disease called pernicious anaemia.

"Glossitic Anaemia" plus "Septic Anaemia" in the same Patient: Importance of Oral Sepsis as a Complication.

In addition to the history or presence of sore-tongue lesions, which I regard as of utmost diagnostic importance, the mouth in glossitic anaemia patients generally presents when first seen another class of infective lesions connected not with the tongue but with the teeth. There are the septic conditions which I term "oral sepsis" (1900). I have kept them apart from the glossitic lesions because they are of a different character and significance. However bad they may be they do not in the absence of sore tongue or its history point to the diagnosis of the idiopathic haemolytic disease, glossitic anaemia. On the other hand, any history of sore tongue, however slight it may be, in an anaemic patient should raise the suspicion of this haemolytic disease, even if little or no oral sepsis is present.

In most cases, however, the conditions of oral sepsis presented when the patient first comes under notice are very bad. Thus to quote only one case:

"Many of his teeth are quite loose, both in the upper and lower jaw; they are all very septic, showing periodontitis, pyorrhoea, and calcareous tartar deposits, and much septic gingivitis, and there are in addition a number of carious teeth and septic stumps. He has neglected his teeth, and has been in the habit of himself pulling them out as they became loose."

A pretty septic story is thus presented by such cases—a story prior to 1900 invariably present in all cases throughout the history of the disease, and still presented in some degree or other by every case when it first comes under notice.

What is the importance of these septic lesions around the teeth? It is, I find, of a threefold character, to which I draw your special attention.

1. *Power of Producing Septic Anaemia.*—The one to which I am specially drawing your attention to-day is the power of chronic streptococcal sepsis *per se* in producing a definite and sometimes extreme degree of the anaemia I have termed "septic anaemia." But important as this is in connexion with the prevalence of oral sepsis and the part it is thus playing in causing all sorts of degrees of anaemia—for example, in young children, young adults, and especially in young girls who are already so liable to anaemia of non-infective nature—this power *per se* of producing anaemia by no means exhausts its special importance as a complication of the haemolytic disease, glossitic anaemia. For in this latter disease the tongue is the seat of lesions which cause cracks and fissures and abrasions of its covering epithelium, exposing it therefore in special degree to any septic infection in the mouth. And when one remembers how constantly the tongue is in movement, expanding and contracting, it must act like a sponge in absorbing the intense streptococcal sepsis present in many cases, thereby favouring the production of septic anaemia. Furthermore, the action of septic infection is to retard blood formation in the bone marrow (a pale bone marrow). It thus counteracts the action of the haemolytic infection, which is to stimulate blood formation (red bone marrow). The removal of the sepsis therefore frees the bone marrow from a markedly depressing influence, and allows the full compensatory powers of the bone marrow free play. The result is shown by the remarkable and increased powers of recovery of the haemolytic disease on removal of the sepsis.

2. *Power of Producing "Septic Gastritis" and "Septic Enteritis."*—In this latter disease oral sepsis plays another important part—the one which first drew my attention to it, and the one which I endeavoured to describe in my first account of this subject in 1900. That part is the power of oral sepsis in inducing unhealthy conditions of catarrh in the stomach and intestine ("septic gastritis" and "septic enteritis," as I termed them)—in the alimentary tract. It is these that constitute the class of "certain favourable conditions" which in my first studies in 1890 I concluded to be necessary for the contraction of the haemolytic infection (a specific one) underlying the haemolytic disease and glossitic anaemia. My studies have fully confirmed the importance of this action of oral sepsis. Prior to 1900 the most distressing features of that disease were the frequency of gastric and intestinal symptoms: the loss of appetite, the distaste for food, the nausea, recurrent sickness and vomiting, the looseness of bowels, or the recurrent and oftentimes persistent diarrhoea which marked the progress of this disease—for example, vomiting every day for two or three months. While symptoms of gastro-intestinal disturbance are still definite features of the disease, I never see nowadays this class in the severe degree I formerly witnessed in every case. All the patients recently under my care have indeed been singularly free from them, except from time to time in slight degree. I attribute this happy result to the removal of all oral sepsis—all teeth from the cases—and to the consequent removal of that factor as a potential cause of gastric and intestinal trouble, or as a potential complication and adjuvant of the action of the specific haemolytic lesions that may be, and in all cases are, present in some part or other of the gastric or intestinal mucosa.

3. *Septic Lesions around the Teeth as Seats of the Haemolytic Infection of Glossitic Anaemia.*—But a third (and in my judgement the most important) part, from a pathological point of view, played by oral sepsis in connexion with the haemolytic disease, glossitic anaemia, is the one I have now indicated. This is that the

lesions around septic teeth, the open wounds connected with septic gingivitis—for example, especially under calcareous masses of tartar—the pyorrhoea, the carious roots, the presence of gold caps or bridges, *et hoc genus omne*, are lesions in which the haemolytic infection of the disease also takes root and by which its persistence in the body is favoured. So important is this that in my observation the first seat of that infection is in all probability in most cases such open septic lesions around the teeth. It incubates itself there, thence spreads to the tongue, which afterwards becomes its special seat, and thence spreads to the mucosa of the stomach and intestine.

In short, the exact pathogeny of this disease—its mode of spread—could not be better described than in the words used by one patient regarding it:

"His illness began with sore tongue; his tongue always got inflamed every three weeks, accompanied by some discomfort in the stomach and lower down, as if he were inflamed all the way down."

Or as another equally well described it:

"Tongue became sore about three weeks ago. The soreness seems to go right through to back passage. It appears to be perfectly well for a time; then a relapse occurs every two or three weeks."

Or as another described it:

"His illness began with sore tongue, quickly followed by yellowish complexion (haemolysis) and great weakness (anaemia). He told several doctors that he thought the sore tongue had something to do with it, but they attached no importance to it."

If this be the character of the haemolytic infection—namely, located in the tongue, mucosa of stomach and intestine, and wakening into activity every two or three weeks—the importance of open septic wounds around the teeth, in the sockets of the teeth, and in the bone around the sockets, as the seats of the haemolytic infection becomes extreme. For this infection is undoubtedly present in the tongue, and must invariably be passing from the lesions of the tongue to the sockets of the teeth. Or, conversely, if preserved in the lesions around the teeth, it must constantly be passing to the tongue (stomach and intestine), grievously aggravating the amount of the haemolytic infection already present.

A *circulus vitiosus* is thus created between the tongue lesions and the oral septic lesions. Therefore this oral sepsis in this great haemolytic disease glossitic anaemia, already characterized by the great persistence of its own infection, is of altogether supreme importance. So great is the part it plays that in my judgement there is no safety from it in this disease except by the radical measure of removing every tooth—whether bad or apparently good—in order to remove all the potential haemolytic infection which may be present in the septic lesions around teeth already diseased, or that may subsequently find root in teeth which, although apparently good at the time, may later on become diseased. I have never failed to see immediate benefit follow the removal of even one or two bad teeth, and great benefit follow the removal of as many as seemed bad or doubtful. But I have never failed to regret, in every case I have seen, when watching its subsequent course—and seeing how persistent the haemolytic infection is—that I have not been allowed to remove all the teeth in the first instance, in order to get rid once and for all of the important potential complication of new seats of infection being formed around teeth as they subsequently become bad.

Frequency of Oral Sepsis in "Glossitic Anaemia."

On this point I have, since I first announced it in 1900, had no manner of doubt—such as many, including not a few teachers, seem apparently to have, judging from what I sometimes hear. Their furthest admission regarding the matter does not go beyond the very guarded and non-committal one that "I am inclined to think there may be something in it, although, of course, not as much as you believe. Why, I have seen cases of pernicious anaemia without any teeth!" (Many such cases are now being seen—since 1900, when the importance of removing septic teeth was first drawn attention to. Further, pernicious anaemia is far more common in hospitals than formerly was the case, for the reason that far more chronic cases are now alive.)

My own doubts have long been dispelled, as theirs also would have been, by the painful and tragic experience I had shortly after 1900 of seeing several scores of private patients in rapid succession in the course of a few years, all of them presenting features of sepsis in the teeth and mouth that were perfectly lamentable. The majority of them were found at death's door, literally sodden with neglected sepsis, in addition to their real severe disease, although on an average they had had their disease on them for about two

years before I saw them. So bad was it that I found it impossible to carry out the measures of antiseptics and removal of septic teeth which were clearly indicated, albeit at that time doubtfully regarded alike by the doctor and still more by the patient. ("It beats me to understand what my teeth have got to do with my disease," as one patient in a desperate state remarked.)

The worst experience was of seeing the great majority of these earlier patients die within an average of three and two-third months from the time of my seeing them. Thus, out of my first group of 44 private cases, death occurred in 35 cases: 14 in less than a month (most of them within a few days), 16 within two months, 21 within three months, 25 within four months, 27 within five months, 28 within six months, 31 within seven months, and 35 within eight months.

That picture represents the severity and character of the great idiopathic anaemic disease which throughout my studies I have designated "pernicious anaemia"—the disease which I find to be distinguished by its glossitic and haemolytic features, the disease to which I therefore now give the title of "glossitic anaemia." Such, however, is not the picture which that disease may, since 1900, present if it be freed from sepsis and the septic anaemia which complicates it. It remains the same disease *sui generis*. But when thus freed from sepsis it presents milder clinical features and a much better clinical course than anything it was ever capable of showing prior to 1900, before the era of antiseptics in anaemia which then commenced.

Increased Powers of Recovery after Removal of Sepsis.

When sepsis is removed what is the result? Are the powers of recovery of this haemolytic anaemia thereby increased? Are the features or course of the disease when freed from sepsis and septic anaemia in any degree modified from that presented by the disease previous to 1900, when I first formulated my conclusions?

My own experience is that they are notably modified. The full true features of this idiopathic haemolytic disease, when thus freed from sepsis, have been presented to me time and again during the past twenty years, as they never were seen and never existed before. The dreadful, hopeless pictures which it formerly presented I never now see in any of my cases in whom I have been able to carry out the full measures of antiseptics I consider necessary. However severe the disease may be—and it is always severe; however sharp its individual attacks may be—and they can be of the severest character (for instance, the patient lying in a state of unconsciousness and coma for a whole week, the doctor giving no hope, and stating that the patient could not last till the morning, as in one of the last cases seen): I have time and again seen the patient recover, as if by a miracle, and restored in two or three months, sometimes even in a month or two, to an appearance of robust health and vigour, with high colour, high blood count (90 per cent.), declaring that he had never felt so well in his life. (In the case above referred to the patient came and reported herself, apparently a picture of perfect health with beautiful complexion and colour, two months after she had been at death's door.)

These results, indicating better powers of recovery of this disease, may possibly, it may be said, be due to improved methods of treatment of the disease—for instance, to the use of salvarsan, neo-salvarsan, novarsenobillon, transfusion, excision of spleen, better methods of giving arsenic, etc., of which one reads from time to time in connexion with the treatment of such cases. But in the group of 150 cases under my care during the thirteen years 1900 to 1913 I have used no new method of treatment other than the antiseptic treatment against gastro-intestinal sepsis, which I recommended for the first time in 1890, and the measures of oral antiseptics which I recommended in 1900. I have only on one occasion injected salvarsan; I have never used the other arsenical drugs of this character; I have never injected arsenic hypodermically; and finally, as regards arsenic, I have never given a dose of more than 5 minims at a time, and my usual dose has been 2 to 3 minims given by the mouth in the form of liquor arsenicalis. If my cases have shown the increased powers of recovery I have above described, as they undoubtedly have, the only new measure of treatment with which their improvement can be associated has been the great, and to my mind the all-important, one of strictest antiseptics above referred to, thereby enabling the disease to manifest its own great powers of recovery when freed from complicating sepsis.

III.—POWERS OF RECOVERY IN GLOSSITIC ANAEMIA.

The outcome as regards the nature of severe anaemias being as I have above stated, the results of the measures of treatment directed to the removal of sepsis may be briefly summed up as follows:

The results show a rapidity, degree, and increasing permanence of recovery of "pernicious anaemia" patients under my care of a very striking character, far exceeding anything that I ever saw before 1900, and much more common now than I ever saw up to 1900.

The rapidity and degree of immediate recovery are indeed most remarkable. Formerly I used to be quite pleased when I got a recovery up to 60 per cent. of red cells in the course of four or five months. Now I am accustomed to see rises of from 20 or 30 per cent. up to 60, 70, 80, and 90 per cent. in periods varying from one month up to three months. I show you a few of these results in eight cases of pernicious anaemia selected almost at random—seven of them from cases under my care during the past year of my hospital work. All the cases show a very immediate and striking degree of blood improvement, as will be seen by the rises set out in the following table:

34 per cent. to 76 per cent. in seven weeks, and then to 88 per cent. four weeks later.
25 per cent. to 78 per cent. in eight weeks, and then to 90 per cent. two weeks later.
38 per cent. to 76 per cent. in nine weeks.
21 per cent. to 78 per cent. in four months.
28 per cent. to 84 per cent. in two months.
27 per cent. to 67 per cent. in four weeks, then up to 90 per cent. four months later, at which level it remained (with three short breaks) for three years, and then continued for fifteen years, when the patient died of another disease.
18 per cent. to 71 per cent. in four weeks, and 102 per cent. in eight weeks.
38 per cent. to 105 per cent. in four weeks.

In comparison with the foregoing I give my experiences in the first 18 private cases I saw (1890-1901) prior to the period of oral antiseptics which I introduced in 1900:

Course of 18 Cases observed, 1890-1901.			
Fatal within 1 month	...	...	8 cases.
" " 4 months	...	...	13 "
" " 8 months	...	...	15 "
" " 1 year	...	...	16 "

Increasing Chronicity of the Haemolytic Disease ("Glossitic Anaemia") as shown by Percentage of Red Cells in 171 Blood Counts in 13 Cases at Various Stages up to 15 Years.			
Percentage of Red Cells.	No. of Counts.	Percentage of Counts.	
105-90	18	10	— 10
89-80	14	8	— 8
79-70	22	13	— 21
69-60	25	14	— 29
59-50	26	15	— 10
49-40	18	10	— 14
39-30	24	14	— 24
29-20	18	10	— 3
19-8	6	3	— 13

I bring out in the foregoing table the most remarkable fact regarding blood changes, probably new to you, to which I draw your special attention. That fact is the increasing chronicity of the disease as shown by the degree of its blood changes. In the mind of everyone the disease called "pernicious anaemia" is specially associated with extraordinarily low blood counts. When we think of it, we think of low percentages of 20 or 30 per cent. causing, as I have had frequent occasion to observe, most extreme alarm. These low counts are undoubtedly presented at some period or other in the course of the disease. But what is not generally known is that these low counts only occur during the acute attacks which characterize the disease, and that these attacks occur generally only once a year. They last a varying period of two to three months. But the acute stage in which the blood count is as low as 20 to 30 per cent. may last only about a month or two; and during the latter part of that period, as I have time and again seen, the patient may be feeling well and on the high road to recovery, even although his blood count remains only 30 to 40 per cent. Moreover, it is during these attacks while the patient is under observation that most blood counts are made.

Bearing the above facts in mind, the most remarkable

result that appears from the above table is that only 13 per cent. of the total counts were below 30 per cent.; 24 per cent. were between 30 and less than 50 per cent.; 29 per cent. were between 50 and less than 70 per cent.; no fewer than 21 per cent. were between 70 and less than 90 per cent.; and finally no fewer than 10 per cent. were 90 up to as high as 105 per cent.

An anaemic disease, in which 31 per cent. of the blood counts in its various stages are over 70 per cent., and 29 per cent. are between 50 and 69—a total of 60 per cent. with over 50 per cent. of red cells, including no fewer than 10 per cent. with percentages between 90 and 105 per cent.: such is the haemolytic disease termed "pernicious anaemia." One might almost say: "Even if one calls it anaemia on account of the degree of anaemia which, when active, it does undoubtedly show, why call it by the ferocious prognostic title 'pernicious,' if, as stated, it may run a course as long as ten to thirteen years, or even longer? Why saddle the sufferer with the unnecessary misery of such a name?"

The facts, in my experience of the disease, are those I have just stated, and the question thus put is one which I think is fully justified. I only know the result—namely, that the dreadful name "pernicious," having been foisted upon English medicine about fifty years ago from German sources, and given to this anaemia, to which English medicine had given the title of "idiopathic" (1855), or still more definitely "most idiopathic" (1822), is still retained, with the result that "it makes the flesh creep" whenever the name is mentioned. It hangs like a gravestone round the neck of the sufferer, not only when he is ill, but also during long intervals when he may not only feel, but actually be, very well.

If this disease throughout its entire course be not characterized by an excessive degree of anaemia, and if the degree of anaemia actually present does not prevent the patient from feeling and being very well, what other name than pernicious can be given to it to indicate that even at the times when blood counts are high (for example, 80 to 100 per cent.) the disease is still present, and may in all probability recur if not continuously watched—some name that in the absence of blood changes may indicate its presence or its possible recrudescence? A name that would in the intervals of recovery give this information and help would indeed be a godsend to the sufferer and the observer. Such a name could in my judgement be given to it—a name connoting one of the chief seats of the haemolytic infective lesions underlying this great haemolytic disease. That lesion is the curious and recurrent sore tongue—one of its earliest and one of its most persistent features—"a most peculiar glossitis," first described by me thirty years ago (1890), characterizing "a most peculiar and idiopathic anaemia."

"Glossitic anaemia" would be the name that would of all others in my experience best connote this great haemolytic disease, help in its early diagnosis even within a few weeks of its onset and in its control by treatment throughout its course, by directing continuous attention to one of its earliest and most constant, most characteristic, and most easily recognized features.

The name "pernicious" which it bears fulfils, on the other hand, not a single purpose connected with the art, science, or practice of medicine. It is false, misleading, hurtful, and harmful; it is mischievous, prejudicial, disadvantageous, disserviceable; it is unlucky, sinister, obnoxious, oppressive, burdensome; it is inauspicious, destructive, and venomous; it is bad, as bad as can be, ill-contrived, ill-conditioned, grievous, deplorable, lamentable, and pitiable; it is wrong, shocking, hateful, detestable, and confounded; it is inadvisable, unprofitable, inexpedient, useless, unskillful, and hopeless.

The measure to which it is all these is such that one of the requests I constantly receive from doctors is not to mention the name of his disease to the patient, as it would unduly alarm him!

If I might be allowed, I would make an urgent appeal to all teachers and writers, in the interests alike of clinical medicine, scientific medicine, the art of medicine, and the practice of medicine, to drive the accursed name out of the nomenclature of diseases, and substitute for it the name which I have finally suggested, which is the opposite of "pernicious"—namely, beneficial, valuable, serviceable, advantageous, profitable, edifying; propitious, hope-giving, fair, genuine, and true; unexceptionable and unobjectionable.

"Pernicious" Traditions.

Such briefly are the features of this disease as revealed to me by my studies for the past thirty-three years—one-third of the total history of the disease. In the case of any other disease of an obscure nature, new facts concerning it would be welcomed, and at once assimilated and incorporated in the body of knowledge regarding it. But in the case of this disease, it may be said that "in vain is any new information

supplied." For the whole ground is already occupied—not by facts, but by firmly rooted traditions, associated not so much with the disease as with the name "pernicious"—pernicious traditions, as they may indeed be correctly termed. These traditions are that the anaemia so called is a mystery: that nothing definite is known about it; that its chief character indeed is that nothing definite can be known about it; certainly that nothing definite can be done for it; that there is little or no hope for its recovery—so little, indeed, that if it does recover it cannot have been the disease. In connexion with it more than with any other disease the current teaching was, and apparently from some recent experiences in examining students still is, expressed in the succinct formula: "Very little is known about this disease"; "Its pathology is not at all known." This teaching has sunk deep into the minds of the profession, and is equally well known to the unfortunate sufferers.

Nevertheless, the actual facts in my experience are that I know of no disease in medicine more clearly defined in all its features from start to finish than this disease; none whose pathology has been more fully worked out in all its many relations (in the blood, liver, spleen, bone marrow; in its striking infective lesions in the tongue; in its neurotoxic lesions and manifestations); none whose mode of onset, features of invasion, and clinical features and progress from day to day, month to month, and year by year, have been made more clear, or can at any time be more clearly and certainly predicted by me. Lastly, I know of no disease whose study has directly or indirectly led to the introduction of new measures of prevention, treatment, or control, applicable not only to itself but to all other forms of anaemia, and to a whole range of other general diseases.

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