Observations

ON

NASAL AND ORAL FOCAL SEPSIS IN THE ETIOLOGY
OF GASTRO-INTESTINAL AND PULMONARY
INFECTIVE DISEASES.*

BY

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(Pathological Specimens and Report.)

THE term "focal sepsis" is usually applied in its clinical sense to established pyogenic infection such as occurs when an initial infective invasion, having overcome systemic and tissue defensive reaction, persists as a chronic localized infection. Nevertheless in patients with nasal passages choked with polypus, or copious purulent gingivitis round the necks of living teeth, or periapical dental abscess, one often looks in vain for systemic complications; the copious outpouring of polymorphonuclears seems a measure of successful local resistance to the focal infection. Chronic bacterial toxæmia and subinfection is most prone to arise from chronic latent focal infections, such as frequently occur in nasal sinusitis, with relatively non-purulent discharge (sinus infection without pus in some degree does not exist), or periapical dental sepsis, often with no pus at all. Hence the existence of a causal focal sepsis in pulmonary or gastro-intestinal infection is often to be discovered only by careful investigation.

Sepsis of the mouth, pharynx, and nose may affect the lower respiratory tract or gastro-intestinal tracts (a) by direct spread of infection along the mucous membranes, through the larynx and trachea; (b) by the blood stream or lymph-vascular infection; (c) by inhalation of septic particles or secretions, or by the swallowing of enormous numbers of organisms.

GASTRO-INTESTINAL INFECTIONS.

Organisms Swallowed.

That patients may swallow immense numbers of septic organisms with impunity is certain, for the normal acid gastric secretion is a potent antiseptic barrier; but if the mass infection is continued it fairly frequently results in gastric catarrh or gastritis, with hypochlorhydria, constipation, diarrhoea, or recurring colitis. It would seem likely that naso-oral infection may originate local gastric or duodenal ulcers; or, by spreading through a relaxed sphincter of Oddi, cholecystitis and gall-stones; or, as more commonly appears to happen, appendicitis. Again, such gastro-intestinal infections may be indirectly determined by toxæmia with resulting endocrine exhaustion.

Infection Conveyed through the Blood Stream.

In such cases pyogenic organisms apparently display an elective affinity for the regions involved—for example, the gastro-intestinal tract—which the researches of Rosenow have gone far to explain and to prove.

It appears, at any rate, a reasonable assumption that, in many cases, a chronic subinfection is commonly set up in the gastro-intestinal tract, although in many a patient a relative auto-immunization renders him merely a "carrier" until, perchance, exposure to cold or some intercurrent factor determines an exacerbation of what is really a long-standing infection. When eight years ago, in 1920, in a contribution to this society, I urged the importance of nasal sinus infection as a causal factor in appendicitis, and also of gastric and duodenal ulcers,¹ an analysis of 90 consecutive cases of sinusitis in my own practice showed that no fewer than 14 had undergone appendicectomy, 2 had operation for duodenal ulcer, and

2 patients had gastric ulcer. Further evidence was included in my 1925 Semon Lecture.

I now turn to quite recent observations of the general surgeon and physician in support of my thesis that naso-oral focal sepsis is to be reckoned among the primary sources of gastric and duodenal ulcer, cholecystitis, and appendicitis. Mr. A. H. Burgess,² writing on chronic ulceration of the stomach and duodenum, after referring to the work of Rosenow and of Wilkie, says that "these researches emphasized the importance of a careful search for any focus of infection in the teeth, tonsils, nasal sinuses, or elsewhere before operation." Professor Wilkie³ stresses the frequent simultaneous association of gall-bladder and appendix infection, "not consecutive but simultaneous blood-borne infections, usually of streptococcal type." Dr. Izod Bennett,⁴ writing on the treatment of gastric ulcer, says that "oral sepsis is probably the most important cause of gastric and duodenal ulcer." As long ago as 1900 Dr. William Hunter⁵ urged the importance of oral and nasal sepsis as causes of serious gastric and intestinal disease. How can one reconcile the large percentage of gastric and duodenal ulcers that Hugh MacLean⁶ cured by "intensive alkaline treatment" with the current view that absolute or relative hypochlorhydria, and therefore diminution of the antiseptic barrier in the stomach normally ensured by the free hydrochloric acid there, leads to the uninhibited swallowed pyogenic organisms infecting the gastric mucosa or that of the duodenum? Are there two distinct groups of gastro-duodenal ulcer—those due to hyperchlorhydria, non-infective, with ulceration from the surface, and those due to blood-borne infection, in which, as in Pickworth's specimens of G. S., the infecting organisms invade the deeper layers of the gastric mucosa and not the surface epithelium? It seems probable that appendix infection results from swallowed organisms, for there the intestinal contents are normally alkaline, while infective gastro-duodenal ulcers are often blood-borne, and thus the frequent concomitance of appendicitis and gastro-duodenal ulcers of infective origin might be explained.

Of the specimens of sphenoidal sinusitis that Dr. Pickworth brings before us to illustrate the purport of this paper, those from G. S. might be justly termed a "human parallel of Rosenow's experiments," for in this case a chronic diplococcal infection has been traced, invading the sinus mucosa from the surface, and spreading to the pituitary capsule and gland; in the same case similar diplococci are also demonstrated in the deeper layers of the evenly spaced haemorrhagic patches in the gastric mucosa. Furthermore, in this and other specimens the diplococcal infection, traced to the pituitary, explains the evidences of endocrine disturbance, since the superjacent hypothalamus is the region held to control many of the basal metabolic processes. (See Fig. 9.) These observations of Pickworth, corroborating similar researches by Logan Turner, Reynolds, and others, point to infection by the blood stream as being the most likely pathway of many sub-infections, rather than infection by inhaled or swallowed organisms. Why organisms in the blood stream should have an elective affinity for certain regions or organs we do not know, but that such elective affinity is shown Rosenow's researches leave little room for doubt. Furthermore, this same elective affinity of certain strains of infective organisms for certain tissues is supported by clinical experience—as, for instance, in epidemic influenza, which in one epidemic tends to involve the lungs, in another the gastro-intestinal tract, and in yet another shows a proclivity to cerebro-spinal complications.

Dr. Pickworth's Specimens of Sphenoidal Sinuses and Gastric Mucosa.

These demonstrate, macroscopically and microscopically, the association of infective conditions of the sphenoidal sinus with (a) lesions of the stomach mucosa, and (b) changes in the pituitary gland. (Several other specimens shown are excluded by limitations of space.)

Specimen G. S.—This shows peculiarly evenly spaced haemorrhages in the stomach mucosa. The haemorrhages are near the surface, superficial to small thrombosed blood vessels. The mucosa, apart from the haemorrhages, is of good colour, the whole

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resembling a leopard's skin (Fig. 1). The thrombosed vessels contain diplococci (Fig. 2), although very sparsely distributed. The sphenoidal sinus (Fig. 3) shows a much thickened membrane containing large masses of cocci invading the deeper tissues, usually without, but occasionally with, lymphocytic infiltration (Figs. 4 and 5). These cocci are apparently identical with those invading the stomach and also the pituitary capsule and gland.

Specimen W. J. (Fig. 6) shows haemorrhages in process of absorption, and represents an intermediate stage between the above specimen and the following.

FIG. 1.—Stomach mucosa (G. S.). Multiple superficial haemorrhages beneath which were thrombosed vessels containing diplococci.

Specimen A. L. (Fig. 7) shows multiple deep pitting—really small ulcers—and an occasional dark area shading off into the surrounding tissue. This is probably an example of resolution of the "leopard's skin" condition, in which the haemorrhages and thrombosed vessels have been digested with accompanying attempt at repair.

The partial resolution seen in specimens W. J. and A. L. indicate that the haemorrhages of G. S. are not merely a terminal condition.

Specimens J. C. and M. R. are examples of sphenoidal sinusitis, one associated with capillary haemorrhages (diapedesis), the other with multiple pin-head lymphocytic nodules in the gastric mucosa. (Illustrations of these specimens not reproduced.)

FIG. 2.—Stomach (G. S.), showing organisms amongst blood corpuscles from thrombosed blood vessel. These organisms are of similar microscopic appearance to those seen in the sinus membrane.

PULMONARY INFECTIONS.

The rhinologist has long been familiar with the anaemia, cough, expectoration of muco-pus, sometimes streaked with blood, loss of appetite, wasting, nocturnal fever, and sweats that may occur in chronic purulent nasal sinusitis, often with localized bronchitis, and while in earlier and less marked cases early tuberculosis is mimicked, in old-standing cases they rather suggest advanced pulmonary tuberculosis. Moreover, these chronic septic sinuses are prone to cause recurrent pulmonary infections, till in turn a subinfection of the lung becomes a chronic focal infection. Dr. Young⁷

says very truly: "Nasal sepsis may give rise to symptoms and signs curiously mimicking those of early apical tuberculosis—with definite signs in the lungs, particularly at the apices, which clear up when the nasal condition has been effectively treated."

My experience of sinus infections leads to the conviction that in many patients with constant recurrence of bronchitis the source of infection lies in the chronic sinusitis, where the established infection with relative auto-immunization renders the patient a sinus "carrier"; in

FIG. 3.—Sphenoidal sinus (G. S.). The mucosa was thickened and showed invasion by organisms. (See Figs. 4 and 5.)

course of time the same seems true of pulmonary sub-infection, when the patient becomes a lung "carrier."

We know that in chronic pyogenic infections of the mucosa of the sinuses the organisms may invade the sub-mucosa and, with quiescent intervals without symptoms, activate from time to time under the influence of climatic conditions or the symbiosis of a hetero-infection—as, for instance, influenza, measles, etc. There is reason to believe the same obtains in pulmonary infections, and this explains some of the pulmonary complications following general anaesthesia, which are not by any means always due to infection from above, but may be due to sensitization

FIG. 4.—Sinus membrane (G. S.), showing masses of organisms invading the membrane.

of pre-existing lung infection, though any established focal sepsis in the nose and mouth is a constant menace to the lower respiratory tract. It is hardly necessary to discuss the recognized fact that tonsillar sepsis or tuberculosis may spread to the hilum and peribronchial tissues of the lung, and it appears certain that lung complications of a nasal sinus infection are often the result of blood stream infection.

Familiar experience of the catarrhal infection known as the common cold illustrates the tendency of the naso-oral catarrh to spread to the lower respiratory tract, particularly in certain individuals whose colds always spread to the

chest; in these there is often an acquired liability to frequent recurrence, and, moreover, in the same pulmonary area each time. Now, as Batty Shaw⁸ observes, we are not sure the recurrent attacks in such patients are the result of reinfection from outside, while many become chronic bronchitics, and are, in fact, "carriers." "The infection is a reinfection from within."

That bronchiectasis is very frequently due to secondary infection from naso-oral sepsis is now accepted, and it is probable that early and less marked forms of bronchiectasis are not seldom present, when signs and symptoms are as yet too indefinite to permit of an exact diagnosis, perhaps due to pressure in coughing acting on a bronchial musculature and tissues weakened by infective processes.

It should hardly be necessary to emphasize the importance of recognizing and removing focal infection of the mouth or nose in cases of pulmonary tuberculosis. But there would seem to be good grounds for suspecting that sometimes patients with such focal infections, with pulmonary complications diagnosed as phthisis, despite the failure to find tubercle bacilli in the sputum, are in reality not tuberculous at all, but examples of sepsis infection. Such pulmonary cases may be clinically indistinguishable from the so-called phthisis without tubercle bacilli; they benefit greatly, and may become cured by sanatorium methods; but such methods are immensely assisted by the recognition and removal of the causal focal infection, without which every method of treatment is prone to prove abortive.

Curiously enough, reports on the sputum, which may be teeming with virulent pyogenic organisms, are usually returned "negative" unless a few stray tubercle bacilli can be identified, often only after repeated examination. Yet, even in cases that are truly tuberculous, the association of other pathogenic organisms is by no means a negligible factor. In every case of clinical pulmonary tuberculosis, whether tubercle bacilli are demonstrable or

surgeon, or the laryngologist, yet seldom if ever conjointly. The following are three good examples in which the case-histories suggested focal infection.

The first came under my care last October. He was a man, aged 64, in active pursuance of his profession, which brought him constantly before the public. Apparently fit when I saw him then, he had on so many occasions of recent years been laid up with attacks of febrile nasal catarrh, which "laid him out" and caused severe financial loss, that he was in constant dread of their seemingly inevitable recurrences. Twenty-seven years previously, in 1900, he had left antral empyema due to diseased teeth. These were extracted, the alveolus opened, and a gold tube inserted; through this daily lavage was carried out for about ten years, when, being considered no longer necessary, the tube was removed and the opening allowed to close. Two years later, in 1912, he consulted a colleague for sensations in the antral region, but transillumination was negative and he was reassured. Again, four years later, occasional colds and laryngitis and slight cacostmia made him seek a further consultation; but once more transillumination and likewise a skiagram were both negative. In 1921, with a severe febrile attack abroad, he had a septic abscess on his foot, and again in 1922 and 1923 slight cacostmia.

In January, 1923, he underwent appendicectomy in London for acute appendicitis, and five weeks later an operation on his gall-bladder was performed by the same surgeon.

In April, 1927, he felt and looked ill and neurasthenic. He could not concentrate, and had difficulty in memorizing, which for him in his work was most unusual. A few weeks later he had a severe feverish cold; he was in bed ten days, as he had a pneumonic patch and rusty sputum—streptococci were cultured from a pharyngeal swab. Regaining his relative auto-immunization he returned to work; but six months later, though in fair health, he was still in constant dread of further breakdowns.

Now the history of his recurring febrile colds, appendicitis, cholecystitis, and phases of poor memory, pointed so strongly to a focal infection that, despite the absence of any nasal abnormality or catarrh, using the suction syringe, exploration of the left antrum revealed a pure growth of pneumococcus with slight phagocytosis, though his right antrum was sterile. It would seem that this pneumococcal focus was the causal factor of his septic pneumonia, probably of the previous appendicitis and cholecystitis, and likewise of the recurring febrile attacks that had proved so disastrous in his career. Yet his various medical attendants had apparently failed to inquire for those data in the long history which, taken as a whole, seem to afford such a useful diagnostic guide.

FIG. 5.—Sinus membrane (G. S.), showing organisms invading membrane with cellular reaction (the large dark masses are lymphocytes).

FIG. 6.—Stomach mucosa (W. J.). Haemorrhages as in Fig. 1, but showing early stage of resolution.

not, careful inquiry for the existence of focal infection ought never to be omitted.

The Importance of Case-History in Focal Sepsis.

It is very instructive to observe how a patient's medical history alone, taken over a long period, may in itself suffice to suggest some chronic septic infection, ever and anon cropping up, with quiescent intervals due to relative auto-immunization, but manifesting its existence by recrudescences which, on each of several occasions, have separately engaged the attention of the physician, the

FIG. 7.—Stomach mucosa (A. L.). Haemorrhages as in Figs. 1 and 6, but showing later stage of resolution. Many haemorrhages have entirely disappeared, leaving superficial erosion and deep pits.

Miss D., aged 46, suffered from chronic rheumatoid arthritis in shoulders, wrists, fingers, and knees, of twenty-seven years' duration, beginning at the age of 14. She also had chronic rhinitis of much the same duration, yet, although she consulted laryngologists, there was never sufficient evidence to warrant any operative treatment till 1916, when the sphenoidal sinuses were proved to be infected with *Staphylococcus aureus* and *Streptococcus brevis*. Meanwhile, however, she had recurring colitis, and removal of the appendix was followed by pneumonia. From the time her sphenoidal sinuses were opened and drained the arthritis definitely improved and her health has remained uninterruptedly good ever since.

W. M., aged 29, had severe influenza in 1901, appendicitis in 1903, and appendicectomy in 1907, followed by prolonged insomnia and mental depression. He returned to work, but in 1911, after a mild attack of influenza, headaches, and depression with suicidal impulses, culminating in delusional insanity, he was again unable to work. He was found to have staphylococcal infection involving all his nasal sinuses. The sinuses were radically operated on to eliminate all the focal sepsis, and after some months he

FIG. 8.—Sphenoidal sinus (M. L.), showing perforation of pituitary fossa from sphenoidal sinus. Note especially the bony ridge within the fossa indicative of long-standing infection.

lost his delusions, regained his mental balance, and returned to work. He remained in uninterrupted health, and has occupied the position of bank manager for sixteen years.

These three cases, after a long history of nasal infection with ever-recurring complications—extending over several years, and including arthritis, appendicitis, pneumonia, neurasthenia, and insanity—completely recovered, and the oft-recurring infections abruptly ceased with the removal of what certainly would appear to have been the common causal factor of all their illnesses, nasal, pulmonary, and abdominal. The appendicitis cannot be regarded as mere coincidence, and each case in its entirety is a clinical picture representing the long-drawn-out history of a chronic low-grade focal infection.

Now, if these naso-oral focal infections do cause such serious complications, their early recognition and prompt

FIG. 9.—Pituitary stalk (M. L.), showing diplococci at a, b, and c. This suggests a new path of infection of the hypothalamic region of the brain from a sphenoidal sinusitis.

removal may prevent these subinfections of the pulmonary and gastro-intestinal tracts, for a latent focal infection is truly "a wolf in sheep's clothing." How much serious illness could be prevented by regarding chronic septic infections more seriously without waiting for dangerous complications to point the moral!

If I have wandered into the domain of the physician and surgeon my purpose has been to show how even the rhinologist, ploughing his lonely furrow, is by his work so interlinked with his colleagues that no territory can be regarded as lonely, and that in medicine there is but one field, which ever calls for team work.

REFERENCES.

- ¹ *Practitioner*, April, 1921. ² *Ibid.*, July, 1900. ³ *British Medical Journal*, November 26th, 1927, p. 989. ⁴ *Ibid.*, March 24th, 1928, p. 482. ⁵ *Ibid.*, February 4th, 1928, p. 168. ⁶ *Ibid.*, April 14th, 1928, p. 619. ⁷ *Proc. Roy. Soc. Med.*, xxi, No. 5, 1928. ⁸ *British Medical Journal*, December 26th, 1925, p. 1212.

AN OUTBREAK OF PARATYPHOID B FEVER PRESENTING NOVEL FEATURES.

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THE subject of the present study was a limited outbreak of paratyphoid fever which occurred in May, 1925, in a preparatory school, and which, in certain aspects, presented novel features. The boys, numbering sixty, re-assembled for the summer term on May 5th; some ten days later cases of fever began to occur, and continued to do so till May 29th, when the epidemic ceased. In all, twenty-three cases were notified, while none of those attacked was dangerously ill. The incubation period of this particular epidemic could be accurately ascertained as being from ten to twenty-four days.

The early symptoms were not of a serious nature; for the most part they consisted of a transient headache and a high temperature (102° to 104° F.), coupled with an extraordinary appearance of well-being. At first the headache, the high temperature, and the relatively slow pulse suggested influenza. By the fifth day from the commencement of the epidemic "rose spots" were already visible. At this time, too, a positive agglutination to *B. paratyphosus* B was obtained, and a blood culture performed gave a positive growth of this organism. The diagnosis was therefore clinched.

CLINICAL SYMPTOMS.

In contradistinction to other zymotic diseases the absence of any distressing features at the commencement of the illness was a point to be noted. Save for a few days at the end of the first week appetites and spirits appeared to be unaffected. In the early stages this very absence of symptoms may be misleading and cause delay in diagnosis. The pulse-temperature ratio was typical of the enteric group. In one boy with a temperature of 105° F. the pulse rate registered 100, in another with 101° F. it was 80, and in a third with 104° F. it was 96. In one-fifth of the cases transitory dizziness was complained of, and in 15 per cent. there was vomiting. In one only was there a rigor, and, with the exception of headaches, no other complaints. The onset of the paratyphoid fever was sudden; there were no prodromal symptoms. Constipation was the rule, and the motions did not in the least betray the nature of the illness. The tongue was coated with a thick white central fur. In only one case, a boy with a temperature of 105° F., was mild delirium noted.

The Exanthem.—The first spots appeared at the end of the fifth day; after that 75 per cent. of the cases developed a roseolar rash confined to the chest, abdomen, back, and flanks. In one case the rash was so generalized that the body was covered, with the exception of the soles of the feet, the hands, face, and neck. In 25 per cent. no rash whatever developed, and in a few instances its appearance was delayed till the fourteenth day.

Pyrexia.—In typical cases the fever was of a remittent type for fourteen days; in some cases for seventeen or eighteen days; in the milder forms it lasted from seven to ten days. Defervescence took place by lysis. Palpable enlargement of the spleen was noted in every case from the fifth day onwards. In some the splenomegaly was obvious, and extended four fingerbreadths below the costal margin. In a third of the cases epistaxis was noted. No complications were observed save a severe general myalgia and cardiac dilatation in one boy who had previously suffered from an enlarged heart. Bronchitis and pulmonary complications were completely absent.