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ADDRESSES AND ORIGINAL ARTICLES

ON CERTAIN SEPTICÆMIAS
DUE TO ANAEROBIC ORGANISMS *

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THE septicæmias dealt with in this address arise from several species of anaerobic organisms which are specifically distinct from one another but which possess the common character of living as saprophytes in the natural cavities of the human body, mouth, pharynx, intestine, and genito-urinary passages; they are fragile, very slightly motile, and grow sparsely on culture media. To this group of organisms belong those Gram-negative and non-spore bearing bacilli which certain bacteriologists group together under the name of "bacteroides"; their rôle in the production of non-traumatic gangrene has been described in France by Veillon, Zuber, Rist, Guillemot, and Hallé. With them must also be placed certain Gram-positive anaerobic micrococci, streptococci, and staphylococci, which have been variously named by the different authors describing them.

These septicæmias arise from inflammatory or suppurative lesions in the tissues or cavities where the above-mentioned anaerobic organisms exist under physiological conditions. Having proliferated in these localities they pass into the blood stream and frequently give rise to septic emboli in distant areas. Such septicæmias tend to arise—

- (1) From inflammatory lesions of the nasopharynx, particularly tonsillar and peritonsillar abscesses.
- (2) From similar lesions of the mouth and jaws.
- (3) In connexion with otitis media or mastoiditis.
- (4) From purulent endometritis following parturition.
- (5) From appendicitis.
- (6) From infections of the urinary passages.

But whatever their origin, they present certain common clinical aspects which enable them to be grouped together. For that reason, as typical of the group as a whole, the post-anginal septicæmias will be first described, and in later portions of this paper attention will be directed to the clinical and pathological similarity between such post-anginal septicæmias and those which arise from other sites.

The post-anginal septicæmias due to anaerobic organisms most frequently seen in Paris are due particularly to the *Bacillus funduliformis*, described in 1898 by Jean Hallé, which can usually be isolated in pure culture from the blood and from secondary abscesses; it is sometimes associated with an anaerobic streptococcus. The first cases of septicæmia from this cause were described in 1929 and 1931 by Prof. Pierre Teissier and his collaborators Jean Reilly, Rivalier, Layani, and Stefanescu; later similar observations were published by the writer with Jean Reilly, Layani, Friedman, and André Meyer, by Cathala, Bourgeois, and Gabriel, by Jame and Jaulmes, and by P. de Font-Réaulx. In 1935 Pham Huu-Chi published a considerable work on this subject.

In Germany, where Schottmüller must be given the credit of being the first to describe them in 1918, the importance of the anaerobic post-anginal septicæmias has been emphasised by a number of

physicians, including Buigold, Fränkel, Claus, and Kissling. The name given by them to the usual causal organism of such septicæmias is *Bacillus symbiophiles*, and they state that it is usually associated with an anaerobic streptococcus. The present uncertainty concerning the classification of anaerobic organisms and the diversity of bacteriological tests employed by different observers to identify them make it possible that *B. funduliformis* and *B. symbiophiles* are either identical or else belong to very similar species of bacteria. In any case the description which the German authorities give of the post-anginal septicæmias corresponds feature by feature to what the present writer has observed.

Clinical Picture

The disease usually affects young adults or adolescents, both sexes being equally attacked. Claus and Kissling have observed that sometimes small epidemics occur, a fact which I can confirm. The most usual initial cause is a tonsillar or peritonsillar abscess, opened too late or to an insufficient degree. At times what appears to be a simple tonsillitis may conceal small foci of suppuration in the depths of the tissues which cannot be demonstrated clinically; an example of this was recently under my observation at the Claude Bernard Hospital in Paris.

Since the original work of E. Fränkel in 1919 German authorities have considered that these septicæmias are the result of a thrombophlebitis of the tonsillar and peritonsillar veins which can spread to the internal jugular vein or even to the facial vein. My own observations agree with this conception.

The first symptom of septicæmia complicating the pharyngeal inflammation is a notable rise of temperature to 101° or 103° F., accompanied by an intense rigor. The rigor usually occurs on the fourth or fifth day after the beginning of the sore-throat, occasionally as late as the eighth, tenth, or even twelfth day, by which time the tonsillar inflammation appears to be cured and the initial fever has disappeared. After this rigors are repeated daily, several times per day, or at more remote intervals. In the gravest cases the temperature remains in the region of 100° to 103° with exacerbations corresponding to the rigors; in milder and more chronic cases the pyrexia is hectic and irregular.

There is usually painful swelling of the glands below the maxillary angle usually on one side only, occasionally on both; there is slight local œdema and tenderness on pressure and on movement of the head; this occurs on the lateral aspects of the neck, parallel to the sternomastoid muscle, and extends from the angle of the jaw to the clavicle; suppuration sometimes occurs at this site.

The *B. funduliformis* septicæmias observed by myself have never been pure septicæmias, they have always been accompanied by the formation of distant metastatic abscesses. Amongst such secondary localisations the most frequent are those in the lungs. They occur early and may be present from the first day. They are in the nature of septic infarcts leading almost invariably to multiple abscess formation which is announced by intense thoracic pain of sudden onset, by dyspnoea, sometimes by blood-stained or rusty sputum, by pleural frictions, and by localised areas of subcrepitant râles. Very frequently these pulmonary infarcts are complicated by purulent pleural effusions containing *B. funduliformis*, but in

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rare cases such effusions may be serofibrinous and aseptic. These purulent effusions occasionally open spontaneously into a bronchus, giving rise to a pyopneumothorax.

Articular lesions are also extremely frequent; they range from simple pains in the joints, sometimes of great severity, to suppurative arthritis occurring especially in the shoulders, elbows, knees, sternoclavicular or sacroiliac articulations.

Icterus and subicterus have often been noted and urobilin is invariably present in considerable quantities in the urine.

Renal lesions are manifested by albuminuria, sometimes accompanied by a slight or considerable increase in the blood-urea. I have also had occasion to observe thyroiditis, suppurative peritonitis, abscess formation in the psoas muscle or in the deep muscles of the buttock originating from sacroiliac arthritis. During the course of the disease there is usually a leucocytosis ranging from 13,000 to 30,000 white cells and in the more chronic cases the red cells are sometimes reduced to 2 or 3 millions.

These septicæmias may progress rapidly and end fatally in from 7 to 15 days; in such cases the temperature remains constantly high, the patient is in a state of extreme prostration with the aspect of a case of typhus, and dies in coma. In other cases the repeated recurrence of attacks of extreme high temperature may in a few days bring about fatal collapse. Again the fatal termination may be delayed to the end of the third week, or even a month or six weeks may pass before it occurs. In such examples the temperature becomes irregular and oscillating; in accordance with the recurrence of excessive febrile attacks one sees the usual phenomena appear; pulmonary infarcts, pleural effusions, and arthritic phenomena; the patient wastes, the colour becomes pale and earthy, and there are profuse sweats; finally delirium occurs and death follows in a condition of cachexia. It may be hastened by the sudden bursting of an abscess into the bronchus followed by syncope.

Diagnosis

The most characteristic lesions found at autopsy are those in the respiratory tract. The lungs are the site of necrotic infarcts, both centrally and peripherally, usually about the size of a pigeon's egg and circumscribed. Some are seen as yellow masses surrounded by a hæmorrhagic zone, others in the form of cavities containing pus. From these lesions *B. funduliformis* can usually be recovered in pure culture, but occasionally it is associated with an anaerobic streptococcus. In a case recorded by Prof. Tessier and his co-workers, which was accompanied by deep jaundice and purpura, the liver was greatly enlarged and was studded with necrotic abscesses from which the organism was isolated in pure state.

From this it is clear that these septicæmias carry an extremely grave prognosis. Of the 20 cases observed by the writer and certain of his colleagues in Paris only two have recovered. These two were, however, amongst those appearing most ill and were complicated by pulmonary and arthritic manifestations; further, the number of organisms in the blood, estimated after the examinations of cultures, appeared as great in these as in the fatal cases. In these survivors cure occurred spontaneously and treatment had been of purely symptomatic character.

It is therefore understandable that certain German observers have been led, as soon as the clinical diagnosis was possible, and without awaiting the

results of bacteriological examination, to perform ligation of the internal jugular vein on the side of the affected tonsil. They claim that thanks to this intervention the mortality has been diminished. I have personally had recourse to this treatment in a recent case but unhappily without success in preventing a fatal termination.

To anyone instructed as to the nature of these septicæmias it becomes relatively easy to make a diagnosis on the simple clinical findings. The appearance and repetition several days after the onset of a sore-throat (and particularly of a tonsillar abscess) of severe pyrexial attacks with an initial rigor, or still more certainly the occurrence of pulmonary infarcts and arthritic manifestations, constitute a syndrome so characteristic that mistake is almost impossible.

Certain diagnosis is established by bacteriological examination. *B. funduliformis* is easy to discover in the purulent effusions, but it is blood culture on anaerobic media which gives the earliest definite information, and this is particularly sure if the blood is taken during a rigor.

The culture medium employed at the Claude Bernard Hospital by J. Reilly, which can be particularly recommended, consists of 10 c.cm. of the glucose agar of Veillon to which is added 40 c.cm. of peptonised bouillon and 2 c.cm. of a 20 per cent. solution of glucose. This medium divided in glass tubes 25 cm. long and 25 mm. wide, is liquefied by heat at the moment of employment and kept at a temperature of 40° C. After 2 to 4 c.cm. of blood have been added the tubes are immediately cooled under the tap. The colonies appear in it after two to four days' incubation at 37°.

B. funduliformis in pus smears appears in the form of a fine bacillus of 2 to 3 μ in length, Gram-negative, and exhibiting at each end a well-coloured mass, whilst the centre of the microbe remains clear. In cultures it presents, and this is a very important point, a remarkable polymorphic appearance. It occurs in preparations simultaneously as a fine bacillus, as long filaments, more or less voluminous, and sometimes as spherical elements. Some of these spherical bodies, of a diameter of about 2 to 4 μ , are intensely susceptible to basic stains. Others achieve greater dimensions, as much as 12 to 14 μ . Their protoplasm is clear but they contain coloured nuclei of various shapes sometimes resembling the nuclei of polynuclear leucocytes. The spherical elements are quite characteristic and permit absolute identification of *B. funduliformis*. The polymorphic character of the microbe elements may be observed in the first cultures obtained from the blood but is much more obvious in subcultures. In individual cases sometimes the forms with filaments and sometimes the spherical forms predominate.

One further characteristic of the bacillus may be mentioned—namely, that it is constantly hæmolytic. Finally, J. Reilly has demonstrated that, on injection of cultures into the rabbit, septicæmia with metastatic abscess formation in the lungs, liver, and joints, exactly comparable to what is seen in man, is produced.

Various Sites of Infection

THROAT AND EAR

The *B. funduliformis* is the commonest pathogenic agent in post-anginal septicæmias such as have been described above. But other bacilli of the same group may also be the causal agents. Allusion has already been made to the *B. symbiophiles* of Schottmüller; recently Grumbach and Verdan (of Zürich) have in three instances found in the blood a "fuso-bacterium nucleatum" which is perhaps identical with *B. funduliformis*. There is, on the other hand, an anaerobic organism very definitely distinct from *B. funduliformis*—namely, *B. fragilis*—which is occasionally

responsible, as the present writer, with Guy and Rudolph, has demonstrated; a similar infection has been observed by Richon, Kissel, and Lepoire.

The infections described above are marked by rigors and embolic phenomena, but it occasionally happens that somewhat similar fevers are observed which get well without any such complications although blood culture has revealed anaerobic organisms; we have, for example, observed cases of this sort from which *B. ramosus* has been recovered and another due to an anaerobic staphylococcus. Such cases are exceptional and are not due to a true septicæmia but to simple momentary and benign bacteræmia. These observations are nevertheless instructive; the transient discharge of organisms into the blood stream during a pharyngeal infection is certainly capable, occasionally, of producing embolic phenomena which may take on the appearance of a local disease in which the original cause is not clear. Such septic emboli may be the origin of certain cases of pulmonary suppuration or of empyema or arthritis, clinically resembling that which has been described in this paper but of lesser gravity because a true septicæmia is not present.

On the other hand, the reason why the complications heretofore described have been straightforward suppuration, but not of a putrefactive character, is that they have been due to pure infection by *B. funduliformis* or at most to this organism associated with an anaerobic streptococcus. The fœtid pus of tonsillar abscesses contains many species of anaerobic organisms, and it is surprising that only one or two of them usually pass into the blood stream. It does, however, occasionally occur that others of these anaerobes may take this course and give rise to septicæmias of mixed origin with putrid embolic foci. I have, for example, described with P. de Font-Réaulx, a case with the usual blood picture but complicated by gangrenous osteoperiostitis of the pubis and gangrenous pulmonary abscesses containing many different species of anaerobic organisms.

The description given of the post-anginal septicæmias is sufficient to allow review of those arising from other primary foci to be very brief. Such are observed in the course of otitis and mastoiditis particularly when fœtid otorrhœa has been present, such fœtor being due to infection with anaerobes. Otitis of this type is very frequently complicated by lateral sinus thrombosis and is the cause of pulmonary emboli.

Anaerobic septicæmia arising from otitis and proved by blood culture has been described particularly by Guillemot (*B. fragilis* and *B. radiiformis*), by Boez, Keller, and Kehlstadt (*B. fragilis*), by Boez, Keller, and Schreiber (*B. ramosus*), by Langeron (anaerobic staphylococcus), and by Franklin and Camb (Gram-negative *B. fusiformis*).

The clinical manifestations of such septicæmias are very closely similar to the picture given of the post-anginal septicæmias. The same picture has been observed by us in connexion with buccal suppuration following the extraction of heavily infected teeth.

UTERUS AND PELVIC ORGANS

Anaerobic septicæmias are well known as complications of postpartum uterine sepsis. The clinical similarity of these to the post-anginal septicæmias has recently been emphasised by A. Schneider. The normal presence of *B. funduliformis* and other anaerobic organisms in the vagina was noted in 1898 by J. Hallé, and in 1902 Jeannin called attention to the proliferation of these anaerobes in the uterine cavity after any severe case of suppurative puerperal endometritis.

In a series of publications since 1910, Schottmüller has given a full description of these septicæmias which are always linked with the presence of peri-uterine thrombophlebitis; fever, repeated rigors, pulmonary metastases, and occasional icterus are the outstanding clinical features. He gives as the commonest cause an anaerobic streptococcus, the *Streptococcus putridus*, which may be associated with other organisms including the *B. symbiophiles*. Similar cases have been observed by myself and by Boez, Keller, and Kehlstadt. In the uterine septicæmias, as in the post-anginal ones, the metastatic abscesses are only fœtid when the infection includes a number of different species of anaerobes.

It has further been noted that similar phenomena may occur after surgical operations on the uterus and pelvic organs, and that apart from septicæmia a simple bacteræmia may occur producing distant abscesses the primary focus of which may be overlooked.

OTHER LOCI

Gangrenous appendicitis is known to arise frequently from anaerobic infections; such cases are sometimes complicated by thrombophlebitis of the mesenteric veins, by pylephlebitis, by liver abscess, and by fœtid subphrenic abscess. In such cases Schottmüller has isolated from the blood streptococci, anaerobic staphylococci, and the *B. symbiophiles*. Nedelmann has recently isolated the last-named from such a case in pure culture. The site of the thrombophlebitis in such cases prohibits the formation of pulmonary infarcts, but gangrene of the lung and purulent pleurisy are occasional complications. The usual high fever and rigors characterise such cases.

In 1899 Cottet noted the presence of organisms of this type, notably *B. funduliformis*, in certain cases of peri-urethral suppuration. Thomson and Beaver have reported a case of septicæmia due to *B. fragilis* in a patient suffering from cancer of the bladder, and another of septicæmia due to *B. funduliformis* following prostatectomy, this last case being complicated by iliac phlebitis and pulmonary metastases.

Summary

No attempt has been made to review completely the literature of the subject, but sufficient has been said to demonstrate that, whatever their primary focus, the septicæmias produced by the anaerobic organisms which occur as saprophytes in the natural cavities of the human body display remarkable clinical similarities. They commence by suppuration in the local site and this is followed by local thrombophlebitis. Considerable fever and intense rigors are the next feature, and these are followed very frequently by septic pulmonary emboli. The syndrome is so characteristic that it permits of diagnosis before bacteriological examination, including blood culture, has provided conclusive proof. The post-anginal septicæmias due to *B. funduliformis* have been specially described, but the same phenomena are observed when such septicæmias of anaerobic origin arise from other initial causes.

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