VINCENT’S INFECTION IN CHILDHOOD

BY

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In his 39th letter dated 17th September, 1688, Leeuwenhoek vividly described and with fair accuracy figured for the first time, certain bacteria which he had found on his teeth. Amongst these may be recognized the micro-organisms subsequently known as Vincent’s, who in 1896 described the fusospirochetal symbiosis in cases of hospital gangrene, and two years later as a cause of pseudo-membranous angina. Vincent attached the greater importance to the fusiform rod, but noted the presence of the spirillum in at least 40 out of the 47 cases of gangrene, and in 15 out of the 18 cases of angina. Neither micro-organism was isolated in pure culture, nor did they appear to be pathogenic to normal animals. He found the fusiform micro-organism in the mouths of 14 out of 28 healthy subjects.

Incidence of Vincent’s infection.—Vincent’s micro-organisms have been found exceedingly hard to isolate and grow in pure culture, so from the bacteriological point of view astonishingly little has been added to these observations. On the other hand, the number of pathological conditions with which it is claimed they are associated has grown. Not only are they probably the causative micro-organisms of ulcerative stomatitis and Vincent’s angina, and were shown by Weaver and Tunnicliffe to play an equally important role in the aetiology of noma; but they were also found by Wyatt Wingrave in over 30 per cent. of his 500 cases of chronic aural discharge, by Pilot and Pearlman in the majority of such fetid discharges, and seem in the child occasionally to give rise to a specific acute otitis. Adam mentions having treated over 30 such cases, all, with the exception of one, in children. Mangabeira-Albernaz collected references to other 30 cases, and Baremberg and Lewis have in particular given excellent clinical histories of this condition in children aged 3, 3½ and 4 years.

These cases are characterized by the profuse fetid and sanguineous nature of the discharge, and the attendant pain. They resist ordinary treatment, but respond readily to arsenical preparations such as...
sulpharsphenamine locally and systemically, or to the instillation of a bismuth preparation such as iodobismuthate of quinine (80 per cent.) in an oil emulsion. So far as could be determined from the few cases recorded the age incidence corresponds in the main to that of Vincent's angina.

A similar sanguineous muco-purulent nasal discharge, while generally associated with diphtheritic infection or with a foreign body, has also been associated with an infection of the nose by Vincent's micro-organisms. References to this condition are uncommon. Shulman17, who reported one case in a child of three years, was only able to find reference to one previous case mentioned by Place16. Two further cases, also secondary to a buccal infection, were reported by de Angelis19.

Cases suggesting a direct spread of these micro-organisms beyond the naso-pharynx into both the lungs and the intestinal canal have been reported. In 1906 Castellani20 reported two cases of bronchial spirochætosis, in one of which the blood showed a mononucleosis (11,000 leucocytes with 21 per cent. mononuclears). In the same year Feldman21 published a series of autopsies in which these micro-organisms appeared to have played an important role; one case being of a boy 4½ years old in whom there had been pulmonary gangrene following noma and fusoo-spirochaetal infection of the lung. Four years later Buday22 added to these observations, and Rothwell23 published in America an account of 'bronchial Vincent's angina,' but it was not until 1926 that Vincent24 asserted the identity of spirochaeta bronchialis with the spirochete of the fusoo-spirochaetal symbiosis. The following year D. J. Smith25 published experimental work suggesting that these micro-organisms also played an essential role in the production of pulmonary abscess.

In infections of the intestinal canal these organisms are rarely found. Although Escherich26 in 1884 had described spirochætes in the stools of infants suffering from infantile cholera, and in 1897 Booker27 had published a very suggestive autopsy on a child aged six weeks, it was, with the exception of Le Dantec's28 publications on 'spirillar dysentery,' not until 1917 that Luger29 began to stress the rare occurrence of the fusoo-spirochaetal symbiosis in infections of the intestines, an aspect of spirochætal infection which he and Silberstern30 have recently reviewed.

Neither the pulmonary nor the intestinal forms of fusoo-spirochaetal disease appear to have the peculiar predilection of the buccal manifestations for children and soldiers, an age incidence which was recognized long before* Vincent's or Plaut's31 description of these micro-organisms.

In 1917 there were, for instance, 261 primary admissions for Vincent's disease among American enlisted men, and in 1918 and 1919 there were 1,762

* For references to early literature and history, see Hirsch34 and Rilliet and Barthez35.
and 4,159 respectively\textsuperscript{32}; but subsequent to the war this peculiar incidence became obscured, and particular attention began to be paid to a number of obscure systemic conditions in which there were notable changes in the blood picture and in which Vincent's disease appeared to play some part. These micro-organisms became associated with cases of glandular or infectious mononucleosis and were present in presumably abnormal quantities in 8 out of 4 Bloedorn and Houghton\textsuperscript{33} cases, who suggested the possibility of a relationship between the two conditions. They were found in 3 cases out of 10 by Longcope\textsuperscript{34}; 4 out of 9 by Downey and McKinlay\textsuperscript{35}; 27 out of 29 by Baldridge, Rohner and Hansmann\textsuperscript{36}; and in 6 out of 12 cases by Cottrell\textsuperscript{37}, who concludes that 'the association of spirilla and fusiform bacillus of Vincent . . . is frequent enough to give rise to a strong suspicion at least of a casual relation.' They were the micro-organisms 'most frequently encountered' in the case reports of angina agranulocytica, with which the literature now began to abound\textsuperscript{38}.

In 1929 Zikowsky\textsuperscript{39} reported a series of cases of Vincent's angina with a mononuclear response, an enlarged spleen, and general glandular enlargement. He suggested that many cases reported as mononucleosis, glandular fever and monocytic angina were cases of fuso-spirillary infection. He considered it improbable, however, that these conditions were in any way related to the acute lymphatic leukæmias which they occasionally resembled so closely clinically. But Warren\textsuperscript{40} in his recent review of 118 cases of leukæmia stated that Vincent's organisms were prominent in 50 per cent. of the cases, and this conjunction of conditions is generally considered to be not infrequent.

Few\textsuperscript{41}, however, have the temerity even to suggest more than a coincidental relationship, though there are many\textsuperscript{42} who believe that in every case a 'leukæmia' follows an infectious malady, whether Vincent's disease or some other condition, and see in the blood changes an expression of the inability of the so stimulated hæmatopoietic system to revert to the normal.

The majority of these cases, totalling a whole series of different associated infections, have been reported in adults (see Donath and Saxl\textsuperscript{43} for a recent review with references).

In 1930, however, two detailed case reports of such associations in childhood appeared. Lundholm\textsuperscript{44} published a case of staphylococcal sepsis in a girl of 3½ years that developed into an acute lymphatic leukæmia. Bonciu and Ionesco\textsuperscript{45} reported the case of a little girl with a hæmolytic streptococcal septicæmia and similar blood changes.

We were particularly interested in this aspect of Vincent's infection in childhood, but while generalizations on the apparent mode of onset of the leukæmias have been made, and individual cases reported, detailed analyses appear to be few in the literature. Ward\textsuperscript{45} gave a statistical review in 1917.
Ramsay\textsuperscript{46}, who recently analyzed the symptomatology of the leukæmias in childhood, noted the absence of any such analyses but himself dismisses initial symptoms and apparent mode of onset in a short paragraph.

Morse\textsuperscript{47} in 1922 discussed the onset of 12 cases of undoubted lymphatic leukæmia. There were 4 boys and 8 girls. In one case the malady developed during convalescence from scarlet fever; another apparently followed a fall. In the other cases there was no apparent ætiology. 'The first symptoms noted were enlarged glands in the neck, vomiting, hæmorrhage, each in two instances; weakness, fever, sore throat, anorexia, pallor and abdominal pain, each in one.'

Poynton, Thursfield and Paterson\textsuperscript{48} undertook a general analysis of 18 cases of leukæmia; 14 of these were diagnosed as acute lymphatic leukæmia, two as myeloid, and two apparently of a mixed type. Of the 14 cases of acute lymphatic leukemia 10 were in boys. 'In eight cases the illness developed so gradually that their duration was uncertain; five apparently followed an attack of pleurisy, pneumonia or bronchitis. In two cases diphtheria was the antecedent, and in one a cold three weeks before admission. In another case there was an alveolar abscess.' They incline to the belief

\begin{figure}
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\includegraphics[width=\textwidth]{graph.png}
\caption{Apparent mode of onset of 40 cases of myeloid leukemia and 60 cases of lymphatic leukemia in childhood.}
\end{figure}
that the solution of the problem of leukaemia lies rather in some peculiar reaction than in the existence of some specific infective agent.

Present investigations.

An attempt was made to determine the mode of onset of leukaemia in the child in a rather larger series. For this purpose, despite the opinion of those such as Gulland who consider differentiation in these acute conditions into lymphatic and myeloid forms to be often illusory and impracticable, we have observed such a distinction in our series and have been impressed by the great rarity of the latter condition in childhood. In Graphs I and II the results of this inquiry are summarized.

Twenty-four of the cases of acute lymphatic leukaemia and four of the cases of acute myeloid leukaemia are taken from the records of the Harriet Lane Home, the Johns Hopkins Hospital, and the rest of the cases from the literature. The mode of onset was found to be protean if often appropriate to the age of the child, diarrhoea and vomiting being common in infancy, and pains in the limbs or abdomen more frequent in older children.

For the season of onset a considerable degree of impartiality was shown, and, while the age of onset differed in the two types, in neither did it conform with the incidence of Vincent's infection; examples of this infection apparently initiating a leukaemia in the child were significantly few.
In Graph III is tabulated in the following order the age incidence of a series of cases of ulcerative stomatitis, noma and Vincent's angina derived from the Harriet Lane Home records and the literature50-56.

It is apparent that so far as these figures, chosen at random, are concerned, this peculiar incidence is definite and confined to a few years in childhood, and that a brief interval separates the period of maximum incidence of each condition. This existence of a definite age incidence confined to a few years implies the operation of some common general factor, and a corresponding simplification of the factors concerned in the production of that disease. The manifestations of Vincent's disease may be classified,

**GRAPH III.**

*Age of onset of Vincent's stomatitis, noma, and Vincent's angina in this order.*

so far as the figures met in our analyses are concerned, into three main clinical groups. In one we have a series of acute manifestations occurring in the mouth and naso-pharynx, and in all these examples there is a definite and similar age incidence. In a second group, on the whole uncommon in childhood, there are local changes in tissues remote from the naso-pharynx. Finally, in a third group, buccal manifestations are associated with obscure general conditions of considerable interest, but here the age incidence, when apparently definite, as in angina agranulocytica (recently reviewed by Hueber57), differs markedly from that of the first group, or else, as in the case of the leukaemias, the association appears to be more marked in the adult than in the child.

We hoped that a clearer knowledge of the factors operative in the first group would assist in the understanding of the role played by this infection in the latter group.
At birth, the mouth of the child is sterile (Campo58), though not infrequently, as Bonnaire and Keim59 demonstrated, it becomes infected in the course of the passage of the head through the vagina. Within a few hours of birth it becomes infected with the majority of common air-borne micro-organisms such as streptococci, pyogenes and salivarious, pneumococci, staphylococci, sarcinae, B. coli and B. subtilis. About the twelfth day, as Brailovsky-Lounkevitch60 points out, ten days or so after the B. bifidus has become predominant in the intestine, S. salivarious becomes prominent in the mouth, though not in a sufficient degree for one to be able to speak of a normal buccal flora. With the onset of dentition a notable change occurs in the mouth of the child, and the micro-organisms found tend to resemble those found in the mouth of the adult and Vincent’s micro-organisms now begin to appear. The frequency with which these micro-organisms are said to be found in the normal adult mouth has varied greatly with different observers. A great deal of this discrepancy can be attributed to the efficiency of the method employed in collecting and examining the material.

The sudden importance this condition acquired during the past war led to a considerable amount of fresh work being undertaken. Reckford and Baker’s61 findings are rather frequently quoted. They found on examining smears from the mouths of 50 normal individuals (soldiers) only one positive result for spirilla and fusiform bacilli. Their results are not in accordance with the results of Semple, Price-Jones and Digby62 who found that in the case of 512 soldiers of all ages from 18-35 years and upwards, fusiform bacilli were present on the gums in 489 cases (95.5 per cent.), and spirochaetes in 488 cases (95.3 per cent.). They conclude that these micro-organisms are normal inhabitants of the human mouth and that in cases of gingivitis and Vincent’s angina they are enormously increased in number. Our few figures point to the same conclusion, and this is indeed the opinion of the vast majority of workers in this particular field 63, 64.

The exact time at which these organisms appear in detectable quantities in the mouth of the child has been the subject of few investigations. Violle’s65 statement that they appear at about the fourth or fifth year as a result of eating earth-contaminated food, and an early paper by Oshima66, were the only two references we were able to discover; yet the peculiar age incidence of this group of diseases under normal conditions suggested that such a determination might prove not without interest, while the findings of Pilot67 and others that these organisms are present in some 82 per cent. of tonsils examined suggested the necessity of including them in any scheme of investigation.

The gums, teeth and tonsils of 168 children were therefore examined for these organisms, adopting for this purpose a special technique, the material being aspirated from the margin of the gums and teeth and from the tonsils by means of a ‘straw’ and rubber bulb, and mixed in $\frac{1}{3}$ c.cm. of normal saline. Drops of this mixture were placed on slides and allowed to dry, fixed
and stained by the Harris\textsuperscript{68} modification of Kliewe stain for spirochætes, and in the first 75 cases, drops were also studied under the dark field. The close identity of our results led us to rely in our later examinations upon the Harris stain alone.

Throughout this work particular attention was paid to the condition of the teeth and gums and to the tonsils in relation to our findings. Enormous quantities of Vincent’s micro-organisms were present in the mouths of children with perfect teeth and gums, who confessedly had never brushed their teeth in their lives; in certain cases where they did begin to brush their teeth regularly these micro-organisms became very hard to detect. They were, however, invariably present in lesser quantities in older children who had faulty teeth and diseased gums, but it seemed to us that this was due

\begin{figure}[h]
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\includegraphics[width=0.5\textwidth]{graph4.png}
\caption{Incidence of Vincent’s spirochate and the fusiform rod about the gums and the tonsils of 168 children.}
\end{figure}

N.B.—The positive findings are in black; each column is made up of four columns representing from right to left Gums:—Spirochete, Fusiform. Tonsils:—Spirochete, Fusiform.

not so much to these specific conditions, as that they rendered a reasonable degree of buccal hygiene impossible.

In Graph IV we have tabulated briefly our results. Vincent’s micro-organisms appear to invade the mouth over the same age period as that in which the maladies, in Group 1, associated with these organisms commonly occur. It is suggested that this is not a simple coincidence, but that Vincent’s organisms, while as a rule non-pathogenic, are so in part by virtue of their host’s resistance, and may be pathogenic at their time of invasion, before balance is achieved. Subsequently this balance may rock, but then it is necessary to postulate a further factor, either, as in Group 2,
the invasion of fresh tissues, or else a lowering of the resistance of the host, or enhancement of virulence; and this would imply, as is indeed generally held, that the manifestations of Vincent's infection in Group 3 are to be considered in all probability as secondary to the general condition.

Summary and conclusions.

The manifestations of Vincent's infection in the child have been summarized and the peculiar age incidence emphasized.

The apparent mode of onset of the acute leukemias in childhood has been surveyed, but little support found for the hypothesis that these conditions were secondary either to Vincent's disease or other septic infection.

The age incidence of Vincent's organisms was determined in the mouths of 168 normal children. It is suggested that this incidence bore a relationship to the age incidence of the maladies associated with these organisms and constituted further evidence in support of the belief that these organisms were but secondary invaders in the conditions of angina agranulocytica, infectious mononucleosis and the acute leukemias.

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