THE
ÆTIOLOGY OF PUERPERAL FEVER.

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THE ætiology of puerperal fever is a subject which has long occupied the attention of observers, and upon which up to the present time no satisfactory conclusion has been arrived at.

By many it has been thought that a close connection exists between erysipelas and puerperal fever,—that erysipelas in short may spread amongst puerperal women as puerperal fever, and on the other hand that puerperal fever may spread in the form of erysipelas; but both Volkmann and Hergenberger regard erysipelas as a separate disease, having nothing to do with the phlegmonous processes of puerperal fever.

Fehleisen¹ has proved beyond doubt the existence of a definite species of micrococcus in the lymphatics of the skin in erysipelas at and beyond the margin of redness. He cultivated this organism on a number of media. On nutrient jelly they were found to grow very slowly as small isolated colonies. Upon inoculating the ears of rabbits extensive redness appeared, which spread towards the root

¹ 'Die Aetiologie d. Erysipelas,' Berlin, 1883.

of the ear, and upon making sections near the margin of redness the micrococci could be detected in the lymphatics. Fehleisen further inoculated seven persons with pure cultivations of the organism; of these six developed typical erysipelas, whilst the seventh was probably protected from a fresh attack, as he had suffered only a short time previously from erysipelas.

More recently the subject has been particularly investigated by Gasserow and Winckel. The former observer reports¹ a number of observations and experiments which lead him to the conclusion that no ætiological connection exists between erysipelas and septic processes in puerperal women. He injected the streptococcus of erysipelas (*a*) into the peritoneal cavities of two rabbits; (*b*) into wounds in the abdominal walls of two others; and (*c*) into the subserous cellular tissue of the peritoneum; in none of these animals did he note any ill effects; nor did he find, upon killing the animals some time after, any pathological changes.

On the other hand Winckel states that from cultivations of the heart's blood of a patient who died thirteen days after parturition from purulent peritonitis and pleuritis, &c., at the same time diphtheritic endometritis and ulceration of the vulva being present, he obtained an organism which he describes as the erysipelas micrococcus of Fehleisen; he also isolated the same organism from the pus present in the peritoneum and pleuræ, and from the spleen, lungs, &c. With these cultivations he inoculated the skin of a rabbit's ear and induced redness; injections into the abdominal cavities of four rabbits produced no result in three cases, in the fourth purulent peritonitis. With white mice his inoculations were always followed by fatal changes evidenced by inflammatory processes in the intestines, enlarged spleen, &c. He fails, however, to say whether the organism was recovered from the heart's blood of these animals.

With a view of further investigating this subject, on the suggestion of Dr Klein, and at the request of the Committee of the Brown Institute, I commenced a series of observations.

¹ 'Arch. f. Gyn.,' xxv, 1887, p. 169.

On the morning of the 18th December, 1886, through the kindness of Dr. Grigg, I was present at the post-mortem examination of a woman who had died the previous evening at the Queen Charlotte's Lying-in Hospital. She was confined on the 9th of December of a live child; on the 11th she had tenderness over the hypogastric region, the abdomen was also distended and tympanitic; on the 12th diarrhoea with offensive stools occurred; on the 14th vomiting; on the 15th, the respirations were hurried, and upon examination of the chest some pleurisy and pneumonia were found at the right base; on the 16th the abdomen was very distended, vomiting incessant, and the face very anxious, and on the 17th she died collapsed.

At the post-mortem examination made nine hours after death the usual morbid appearances were found, indicative of acute peritonitis; large quantities of lymph and turbid serum being present in the peritoneal cavity; a pneumonic condition of the base of the right lung was also present.

To obtain a specimen of blood for purposes of cultivation after the method described by Dr. Klein and used by him always in these cases, I took a capillary glass pipette, and after carefully opening the pericardium I plunged this into the right ventricle of the heart, and in this way obtained a pipette full of blood free from accidental contamination. With this I inoculated a series of eight tubes of nutrient gelatine by passing one end through the cotton-wool plug (previously drawn up half way) into the tube and allowing two or three droplets of the blood to run over the sloping surface of the gelatine, which then by means of the end of the tube were spread more or less uniformly over the surface. I likewise made two gelatine depth cultivations, and two gelatine plate cultivations.

At the same time cover-glass specimens were made of the blood in the usual way.¹ These were stained with gentian violet and examined with a Zeiss' D objective, when micrococci in the form of chains or streptococci were plainly visible.

¹ Weigert and Koch.

On December 20th, that is two days after the inoculation, distinct colonies, varying from eight to ten in number, were visible in each of the surface and plate cultivations, and in the gelatine depth tubes there were also evidences of growth, these colonies being particularly noticeable in one of the surface gelatine tubes, where the four or five droplets of blood had been allowed to run down uninterruptedly from the top of the surface growth to the bottom of the tube.

The following day these colonies were most distinct as small, greyish-white dots, quite isolated, and showing no tendency to become confluent, and in all the tubes these and *no other* colonies showed themselves.

The growths were found to consist of micrococci, and further cultivations were made in gelatine and agar-agar, in broth and in milk.

On the surface cultivation of gelatine the organism grows as a film of numerous non-liquefying, small, greyish-white dots as seen by transmitted light, each distinct, with no tendency to become confluent, being first visible two days after inoculation, and arriving at their maximum growth in the course of ten or twelve days. By reflected light the growths present a whitish or slightly translucent appearance. With the aid of a glass the dots are found to be quite discrete, and although they are all small, some of the colonies appear slightly larger than the others. A number of the older dots show a slight halo surrounding the central dot from which minute points are seen to project. When much older, these dots present a distinctly crenated outline.

The streak cultivation on gelatine shows in from two to three days lines of minute, greyish-white dots by reflected light; the dots are larger in the thickest part of the gelatine, smallest in the thinnest part. By reflected light the growth appears as a distinct streak of whitish and slightly translucent dots, varying somewhat in size.

In the depth of gelatine along the track of the needle numerous closely-packed, minute dots appear, which are

thicker and more opaque in the depth, smaller and more transparent near the surface.

If cultivations be made upon the surface of gelatine slightly tinged by the addition of some aniline dye, *e. g.* Spiller's purple, the organism shows no growth.

In agar-agar made with Brand's essence the organism grows more rapidly, being present as a film of small transparent dots with no tendency to become confluent. As the dots grow older they become surrounded with a halo from which project numerous small dots.

Inoculations into sterilized milk give rise to abundant growth as streptococci. The milk is not curdled.

Broth: In two days after inoculation a slight turbidity occurs, which in a few days passes off, leaving a clear supernatant fluid and a whitish deposit. No pellicle is found, and upon microscopic examination the organism is seen as numerous small chains.

Microscopically the organism is found to be a micrococcus, having a great tendency to form diplococci. Specimens examined from broth or milk show numerous short chains or streptococci.

On December 28th I inoculated two white mice from an agar-agar cultivation and also two guinea-pigs.

On December 31st one of the mice inoculated was found dead. There was congestion at the bases of the lung and of both kidneys; the spleen was also enlarged and congested. I made four gelatine tube cultivations of the heart's blood.

January 1st, 1887.—The second mouse was found dead. The same post-mortem appearances presented themselves. Gelatine tube cultivations were made with the heart's blood.

The guinea-pigs showed slight swelling at the site of inoculation, but otherwise appeared well.

January 3rd.—The tube cultivations of the heart's blood of both mice show characteristic dotted growth.

By repeated cultivations of this growth in the various media, I thoroughly satisfied myself I was dealing with the organism originally obtained from the puerperal patient.

With cultivations of the organism, both of the original and of that obtained from the mouse, I inoculated the ears of four rabbits, and in all cases such inoculations were followed in the course of twenty-four hours by a diffused redness which passed off in the course of two or three days and did not show any disposition to spread to the root of the ear, in this respect differing most markedly from the streptococcus of Fehleisen,¹ as well as from the *Streptococcus pyogenes* described by Rosenbach, although these species are in cultural characters similar, and belong to the same group as a number of other species, e.g. the *Micrococcus scarlatinæ* of Klein.

I made further inoculation experiments upon white and grey mice, both with cultivations of the micrococci obtained from the heart's blood of the mice and in all cases such inoculations were followed by the death of the animal in two or three days, and general congestion of the organs with enlargement of the spleen was detected on post-mortem examination. Again, in this a marked difference is to be noted in the action of this organism and that of the *Streptococcus pyogenes*.

On 29th March, 1887, through the kindness of Dr. Matthews Duncan, I was allowed to take some blood from the finger of a patient at St. Bartholomew's Hospital, who had been confined on the 22nd inst. The notes of the case supplied to me were as follows :

23rd.—Patient very hot and feverish, had two or three rigors.

24th and 25th.—Had further rigors, much headache, nausea, and vomiting.

26th.—Admitted into hospital, when the following note was taken : Patient very anxious, complains of pain over the abdomen, lochia not foetid. Pulse 120, soft ; temp. 101° : had a rigor this morning, when temperature reached 105·4°. Urine albuminous. Complains of pain in the left shoulder and elbow and both knees, which are swollen and tender.

¹ Described most ably by him, 'Aetiologie d. Frysipelas,' 1883.

29th.—Rigors continue. Temp. 106° , pulse 120. Pain and swelling in both shoulder-joints.

31st.—The patient died, but no post-mortem examination was allowed.

I took the specimen of blood in the usual manner, and with the proper precautions. The tip of the finger was first well washed with carbolic-acid solution, and a small piece of tape was then wound round the centre of the finger to cause slight congestion of the tip. With a needle then finger was the pricked and the blood drawn into a capillary glass pipette; with this four gelatine tubes were inoculated.

During my absence from the laboratory for a few days, Dr. Klein had been good enough to attend to these tubes, and on the 31st he discovered evidence of growth in all the tubes, as small, whitish dots. These increased somewhat in size and after a time became crenated. One of such colonies, which appeared larger than the others, was spread out over the surface by means of a platinum wire, and then grew as a film of small, translucent, non-liquefying dots. In no single instance did any other organism present itself.

In all respects this growth resembled that obtained from the other patient. Cultivations were made on gelatine and agar-agar and in broth and milk with like results. Mice were also inoculated with the organism: they died in the same time as those inoculated with the organism obtained from the blood of the first patient and they presented post mortem the same appearances, the organism being in like manner recovered from the heart's blood. The ears of rabbits were inoculated both with the organism cultivation from the patient and from the mouse with similar results, viz. a diffused redness passing off in the course of two or three days.

Portions of the organs of the patient who died at Queen Charlotte's Hospital and of the various mice were preserved in Müller's fluid, and sections were made and stained in methyl blue, gentian violet, and eosin, but I have failed

to detect the organism except in the lung of the patient, which showed a few scattered micrococci.

From the foregoing facts I am led to the following conclusions :

1. That this organism occurs in the blood of patients affected with puerperal septicæmia in considerable numbers in the form of streptococci.

2. That in its cultural characters in various media differences can be observed by which it can be distinguished from other streptococci.

3. That it is a distinct and definite species as proved by its action upon rabbits and mice, although it belongs to the same group as other pathogenic streptococci.

4. That it is not the streptococcus of erysipelas of Fehleisen, its action on the ear of the rabbit being quite different ; the latter producing, in the majority of instances, typical erysipelas.

5. That it is not the *Streptococcus pyogenes* of Rosenbach, not only because of its cultural peculiarities—one of these being the abundant growth of the *Streptococcus pyogenes* upon gelatine tinged with Spiller's purple,—but because of its certain action upon mice and upon rabbits. *S. pyogenes* has no effect upon mice to the extent of some 80 per cent. of cases, and likewise rarely produces any effect upon the ear of the rabbit, and when it does, it is a transitory congestion followed by the formation of an abscess.

(For report of the discussion on this paper, see 'Proceedings of the Royal Medical and Chirurgical Society,' Third Series, vol. i, p. 22.)