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The following case of the œdematous form of anthrax seems worthy of being recorded, on account of the rarity of this form of the disease in this country, and also because of certain other interesting features of the case, namely, acute peritonitis and endocarditis due to the bacillus anthracis. The case has already been briefly referred to by Dr. Flexner in the Johns Hopkins Hospital BULLETIN for May-June, 1895.

C. B., aged 59, a native of Germany, and a laborer in a hair factory, came to the Johns Hopkins Hospital Dispensary on Saturday, May 11, 1895, complaining of swelling of the lids of the right eye. His history was as follows:

*Family History.* His father and one brother died of some lung trouble, the exact nature of which he does not know; one brother died of cancer of the liver. The family history is otherwise negative.

*Past History.* He had the usual exantheas as a child. Denies venereal history, and gives no history of secondary lues. Drinks one glass of beer daily. Does not use tobacco. Had typhoid as a young man, but since that time has always been strong and healthy. He has worked in a hair factory for thirteen years.

*Present History.* Two days ago, while working with South American hair, he scratched his right eye with his hand, as it was itching. The next morning he noticed that the eye-lids were slightly swollen, and itchy, and by this morning they were so swollen that he came to the dispensary.



At the time of the visit the swelling was confined to the lids of the right eye, and was fairly sharply localized; it was cedematous in character, and quite boggy, the overlying skin appearing almost of a natural color. Two small incisions were made, one into each lid, and a small quantity of rather thin, whitish fluid, resembling diluted milk, was evacuated. Cultures upon agar-agar were made at this time, and two days later the tube inoculated showed a pure growth of an organism which resembled the bacillus anthracis, and which upon inoculation killed a mouse in 24 hours. Further tests proved it to be the anthrax bacillus.

The patient was admitted to the hospital on May 13, four days from the onset of the disease. The physician who attended him at his home, from Saturday until his admission on Monday, stated that his temperature had been subnormal during the entire period. On admission the patient complained of nothing but slight pain beneath the right side of the jaw; otherwise he felt perfectly comfortable. He had no headache or malaise. His mind was perfectly clear. The following note was made at this time:

Patient is in bed on his back. Temperature F. 102°. Pulse 132 per minute, regular, volume fair, tension not increased. Respirations 16 per minute, easy. Tongue has a slight white coat. The mucous membranes are of a fair color, not cyanosed.

Both eyes are closed by œdema. On the left side the swelling is not nearly so marked as on the right, the lids being distended by a moderately firm, watery œdema.

The lids of the right eye are much swollen, hard, and tense, and the overlying skin is occupied by several vesicles, varying in size from a pea to a bean, and filled with clear, yellowish serum.

The eyes themselves appear uninvolved.

Over the whole of the right side of the face and neck, and extending up onto the scalp, is a marked œdema of varying consistency; immediately around the right eye it is very hard, and covered by tense shiny skin; over the forehead, neck and remainder of the face, as well as over the implicated scalp, it is much less firm and can be easily pitted by pressure.

The œdema extends across to the left side of the forehead, and occupies the neck as low down as the clavicle. On the inside of the mouth, the right cheek is marked with the imprints of the teeth, and has a yellow-gray sloughy appearance.

The thorax is rather barrel-shaped, but expands well and equally.

The lungs are hyper-resonant throughout on percussion; on auscultation the breath-sounds are clear, but expiration is prolonged.

The point of maximum cardiac impulse is neither visible nor palpable. The heart-sounds are best heard in the fifth intercostal space 3 cm. within the mammillary line. The sounds are rather distant, but apparently clear. The area of relative cardiac dullness is almost obliterated by lung tympany.

The border of the liver is indistinctly felt just below the costal margin.

The spleen cannot be palpated.

The abdomen is natural in appearance, but is universally tender to the touch.

The shins are clean. There is no œdema.

The glands on the right side of the neck are moderately enlarged, and tender. Their consistency cannot well be made out, on account of the overlying œdema.

The glands elsewhere are not enlarged.

May 14, 10 a. m. The patient is much worse this morning. He has had several involuntary passages of urine and fœces during the night. The mind is quite clear, and he answers questions rationally. He complains a good deal of cramp-like pains in the abdomen. The pains are situated in the umbilical region, and are sharp and constant, with occasional acute exacerbations, during which he has a desire to defecate. The abdomen is extremely sensitive to pressure this morning. The spleen cannot be palpated. The pulse at the wrist is almost imperceptible and practically uncountable.

The heart-sounds are extremely distant and feeble.

The temperature has been subnormal since 4 a. m. this morning and is now F. 97°.

The right eye is somewhat more swollen than it was yesterday, and the œdema now occupies the whole of the scalp, and has spread down the right side of the chest to the level of the pectoral fold; it also occupies all the tissues overlying the upper part of the sternum.

The patient gradually sank, and died quietly at 4 p. m. on the 14th.

Before death the œdema had spread further over the left cheek, and had also extended somewhat further down the chest. The patient became very cyanotic before death. There was no respiratory distress at any time. His mind was perfectly clear to within fifteen minutes of his death.

On the morning of the 24th he had three loose watery stools, of a grayish color, and apparently containing no blood.

The urine was passed involuntarily and could not be examined.

Autopsy, May 15th, 18 hours after death, the body in the meanwhile having been preserved on ice. Body 174 cm. long, moderately well nourished, strongly built. Rigor mortis in both extremities. The right eyelids are œdematous, closing the eye; they are congested and glazed, and the epidermis is peeling off. The whole right side of the face, below the eye, is œdematous, and the œdema extends over the head and neck. The left eye and left side of the face are less swollen. The œdema is well marked anteriorly over the neck and clavicles, and can be followed well down on the chest. On incising the skin, above the clavicles, much clear serum-like fluid escapes. The œdema extends beyond the median line to the left, and is immediately evident after incision, extending to the sternum. Subcutaneous fat is moderate in amount.

*Peritoneum.* The peritoneal cavity contains turbid fluid; at least 2000 cc. of such fluid is present in the cavity. The serosa is injected, its reflection lost, the vessels very hyperæmic. Smaller and larger ecchymoses are seen beneath the serous membrane. In the smaller omentum, in the region of the pancreas, a large ecchymosis is seen.

In several situations along the small intestine the serosa is very hyperæmic, or even hemorrhagic, over areas as large as a silver quarter, and at these places the walls of the intestine

are bulged outwards. The tissues about the kidneys and pancreas are translucent in appearance and very œdematous.

*Mediastinum.* On removing the sternum the mediastinal tissues are swollen, œdematous, and contain gas bubbles. The œdema of the mediastinal tissues can be traced downwards from the neck, passing in with the cellular tissue below the clavicle. Large gas bubbles or spaces occupy this tissue.

*Lungs.* Both lungs lie free in the pleural cavities. They are both emphysematous, particularly in the upper lobes, and along the anterior borders, which almost meet in the middle line of the body, anteriorly.

The heart is nearly covered by lung.

On incision the two lungs present similar appearances. They are œdematous and very hyperæmic, the œdema and hyperæmia being particularly noticeable in the lower lobes. There is no actual consolidation.

*Pericardium and heart.* On incising the pericardium there is an escape of gas. No excess of fluid in the pericardial cavity. Both layers smooth and pale.

The heart is not enlarged; its cavities appear normal. The valves show no chronic change; the auriculo-ventricular orifices not perceptibly abnormal. Along the free edge of the mitral valve, and less along the aortic segment, are several small elevations, appearing to be quite recent vegetations, covered by small red clots. The aorta is quite smooth. The heart's flesh friable and pale.

*Liver.* The capsule is free from adhesions. Surface smooth. On section, dark in color, quite cloudy; consistency perhaps diminished.

*Spleen.* Free from adhesions; well up under the costal margin; moderately large; only moderately soft; red in color; pulp abundant.

*Kidneys.* Both alike. Capsule strips off easily. The organs are swollen, the surface almost uniformly congested, the congestion being still evident on section. Striæ are coarse. Glomeruli visible and red. Ureters normal.

*Adrenals and pancreas* appear normal.

*Stomach.* In the pyloric region there is in the mucous membrane a large, deeply congested area, measuring 8x6 cm. in extent. It is not clear that there is a false membrane over it, but some grayish-yellow material adheres to the surface.

*Intestines.* The duodenum is congested uniformly. Beginning in the jejunum, which is less congested, there occur at intervals small, elevated, deeply congested, or hemorrhagic foci. These are quite circumscribed, although the mucous membrane about them is congested. They average 2 mm. in width and project 1 mm. above the surface of the intestine; they do not seem to correspond with the lymphatic follicles. The serosa over them is often the deeply congested, bulged-out portion already described; this is, however, not exclusively the case. These foci are quite numerous in the jejunum, at least 15 being present in this part of the gut alone. At times, two or three were close together, though, as a rule, they were more separated. In the ileum they were also seen, in this situation perhaps a little more separated, but in all as many were present as in the jejunum. In connection with one of these areas in the ileum, what appeared to be a false membrane occurred. If a membrane, it was thin, and easily scraped away. Several of the nodules showed superficial ulceration. There was no relation detected to the lymphatic apparatus, and the nodes were less numerous near the ileo-cæcal valve. The large intestine shows no such localized foci, only a diffuse congestion.

*Mesenteric glands* were swollen, congested, hemorrhagic, and softened.

*Brain and cord* not examined.

*Bladder* contained a small amount of turbid urine; the mucous membrane appears normal.

#### BACTERIOLOGICAL EXAMINATION.

Cultures were made, at the time of the first visit to the dispensary, from the incision made into the upper lid. Cover-slips and cultures were made during life, from the serous fluid from one of the vesicles over the right eye, and also from the blood.

The cover-slips from both the vesicle and the blood showed large bacilli, occurring usually in chains, and morphologically resembling the bacillus anthracis.

The cultures taken on the first visit, and also those from the vesicles and blood, all showed large numbers of gray-white colonies.

Transplantations were made from these colonies, upon agar-agar, gelatine, bouillon, potato, and litmus milk, the resulting growths resembling in every particular the growth of bacillus anthracis, and cover-slips showing large bacilli similar to those obtained from the vesicle and blood.

A mouse inoculated subcutaneously with an oese of the original culture died 24 hours later with local œdema and swollen spleen, and the organism was found in abundance in its heart's blood and other organs.

At the time of the autopsy cover-slips were made from the peritoneal fluid, heart's blood, œdematous fluid in the neck, spleen, kidneys and lungs. Typical anthrax bacilli were present in all these preparations, in the peritoneal fluid associated with pus cells.

Cultures from the heart's blood, spleen, peritoneum, liver, kidney and lung, all showed a pure culture of the bacillus anthracis.

Cover-slips and cultures from the urine were negative. At the time of the autopsy three mice were inoculated subcutaneously:

1. With one oese of blood from the heart.
2. With 2 oeses of urine (the surface of the bladder having first been sterilized).
3. With a small piece of tissue scraped from one of the intestinal nodules.

All three animals died within a short time of one another, about 24 hours later. Autopsies showed local œdema and swelling of the spleen, and cover-slips from the site of inoculation, and from the spleen, showed typical anthrax bacilli.

#### HISTOLOGICAL EXAMINATION.

Sections were made from the heart valve (including one of the fresh vegetations), from the lung, liver, kidney, spleen, stomach and intestine.

*Heart valve.* The valve itself appears to be normal, with the exception of an adherent triangular mass attached to one surface of it. This mass represents one of the small fresh vegetations. It is attached by its base, its apex lying free, the principal points of attachment being at the two angles. At its point of attachment the vegetation consists almost entirely

of fibrin; the body of the mass contains, beside fibrin, granular material, red blood corpuscles, many polynuclear leucocytes, and a few cells of an epithelioid type. The polynuclears and epithelioid cells are not equally distributed throughout the mass, but in certain places form closely packed aggregations of cells.

The valve itself appears to be free from anthrax bacilli, these being limited to the vegetation. Here they are extremely numerous, much more so than in the blood, and are distributed throughout the mass, being perhaps a little more numerous in the cellular masses described above than elsewhere. The bacilli occur at times singly, but are generally in groups or long chains.

*Lung.* The lungs show a moderate degree of chronic interstitial pneumonia, with compensatory emphysema, and some congestion.

The anthrax bacilli are more numerous here than in any other organ; they occur in the blood-vessels of the alveolar walls in large numbers. None are to be seen in the alveoli themselves.

*Liver.* The liver shows some thickening of the capsule and a well marked interlobular cirrhosis. In places there is a marked increase in bile pigment in the cells. A few localized areas of extensive fatty degeneration, with fragmentation of nuclei are seen scattered through the organ.

The bacilli are not very numerous in the liver; when seen, they are in small groups between the cells, evidently in the blood-vessels.

*Kidney.* The surface of the kidney is covered by a slight exudate very similar to that obtained from the peritoneum. It consists mainly of red blood cells, but a few poly- and mononuclear elements are also present.

The organ shows here and there thinning and adhesion of the capsule with localized connective tissue formation. A few fibroid glomeruli are seen. The kidney cells are well preserved, as a rule, but in places, especially in the convoluted tubules, are swollen and granular.

The anthrax bacilli are present in moderate numbers; a few are seen in the exudate on the surface, and they are scattered throughout the organ, being most numerous in the glomerular vessels.

*Spleen.* The chief change in the spleen seems to lie in the accumulation of blood within its tissues; the amount of blood is very large, and is evidently largely responsible for the swelling of the organ. The number of polynuclear leucocytes in the organ is very evidently increased.

The bacilli are found throughout the organ, most abundantly in the Malpighian corpuscles; they appear to lie in the blood spaces.

*Stomach.* The changes here are rather sharply localized in the area situated in the pylorus, the gross appearance of which has been described. There is some slight necrosis of the outer layers of the mucosa all through the section, and a much more marked necrosis in the region of the local lesion.

The lesion consists in a sharply localized infiltration of the mucosa with anthrax bacilli. The bacilli forming this mass evidently originally came by means of the blood current, as deep in the mucosa two blood-vessels are seen, both of which show distinct breaks of continuity, with hemorrhage into the surrounding tissue. The mass of bacteria stretches continuously from these vessels, through the mucosa, to the mucous surface of the stomach, and consists of myriads of closely interwoven bacilli. The mass is not of even width from the surface to the depths, but spreads out widely in two places, one immediately beneath the mucous surface, and the other midway between the surface and the muscularis mucosa, thus forming two spreading masses connected with each other and with the ruptured vessels by comparatively thin pedicles of bacteria.

The mucous membrane surrounding this mass is very necrotic, though there is but little reaction, only a few polynuclears being seen about the focus.

*Intestines.* In the diseased areas, described macroscopically, the intestinal wall is much thickened.

The surface epithelium in these areas is almost entirely destroyed, and in many instances the villi have also disappeared, their bases remaining on the level of the openings of the follicles of Lieberkühn. The denuded surface thus left is ragged, but is practically free from exudate of any description. The villi which remain show two distinct processes. A

certain number of them show a markedly more cellular connective tissue than normal, the increase in cells being of the lymphoid variety, and perhaps being only apparent, as the tissue is much compressed from the dilatation of the central vessels.

Certain others of the villi show a necrotic appearance, their cellular elements being greatly reduced in number, the nuclei of the cells which remain staining poorly, and the mass of the affected villus having a hyaline appearance and staining sharply with the eosin. This necrotic process on the surface of the intestine is not confined to the mucosa immediately over the diseased foci, but is found on the surface of the intestine elsewhere.

The muscularis mucosa is seen as an indistinct line, the indistinctness being due to its infiltration by cells, most of them polynuclear leucocytes, which spread apart its fibres, and render its distinction from the submucosa difficult.

In places it is pushed up towards the mucous surface, by the much dilated blood-vessels of the submucosa; in places it is pushed down towards the submucosa by the dilated vessels in the mucous coat.

In the submucous coat the most marked changes are seen, these changes being responsible for most of the increase in thickness of the intestinal wall.

The blood-vessels are intensely dilated and full of blood, in which it is easy to see that an excess of polynuclear leucocytes exists. In places there has been actual rupture of the vessel-wall, with extravasation of blood into the surrounding tissues.

Surrounding the blood-vessels, and filling up the entire area between the muscularis mucosæ and the internal muscular coat, is a dense cellular mass, thickest at the centre of the diseased area, and gradually shading off at the periphery into approximately normal tissue. The return to normal is more rapid towards the peritoneal than towards the mucous surface.

The mass consists almost exclusively of leucocytes with polyform nuclei, as a rule, densely packed, but, in places, separated by masses of granular or fibrillar fibrin.

Towards the mucous surface of the intestine the cellular

infiltration practically stops at the muscularis mucosa, this structure containing only a moderate number of leucocytes, and but a very few being found in the mucosa.

Passing towards the serous surface of the intestine, we find that the polynuclears have passed between the fibres of the circular muscular coat, in places spreading these fibres widely apart by their accumulation, and have penetrated into and through the longitudinal coat, appearing in large numbers on the serous surface of the intestine.

The longitudinal coat contains, in places, large numbers of the pus cells.

Here and there, throughout the cellular mass in the submucous coat, are small areas of necrosis with nuclear fragmentation.

The cell infiltration in the submucous coat is, as a rule, diffuse, but in places it appears as small circumscribed nodules.

These nodules, under the low power, strongly resemble the normal lymphoid follicles of the intestine, the resemblance being made more striking by their situation in the submucous coat, and pushing up to, though not into the mucous coat. Under the high power, however, they are found to be made up of polynuclear leucocytes.

The nodules then are small, round or oval areas of cells situated about in the normal position of the lymphoid follicles, but having no relation whatever to these follicles, as their structure proves, and being in fact focal inflammatory lesions.

The collections of ganglion cells, both in the submucous coat, and between this coat and the internal muscular layer, are widely separated by the wandering in of polynuclear leucocytes between the cells.

The lymphatic vessels just beneath the muscularis mucosa are in places widely dilated, and crowded with bacilli.

In places on the peritoneal surface is an exudate composed of many red blood cells, a good many polynuclear leucocytes, a few mononuclear leucocytes, and fibrin.

The anthrax bacilli are found in all portions of the intestinal wall, though in greatest number in the submucosa.

The necrotic areas on the surface of the mucosa show very large numbers of bacteria; in the majority of instances, how-

ever, these do not appear to be anthrax bacilli, but a much shorter bacillus, though an occasional long bacillus resembling anthrax is seen.

In places, however, on the necrotic surface, masses of practically nothing else but anthrax bacilli are seen.

In the deeper parts of the mucosa, both the anthrax and shorter bacilli are seen, the anthrax bacilli being more numerous near the surface.

In the submucosa the bacilli are numerous; they are scattered throughout the inflammatory areas in small groups, and are found in large numbers in certain regions, viz.:

1. In or immediately beneath the muscularis mucosa in the form of a band of bacilli, closely woven, of about the normal thickness of the muscularis mucosa. Those immediately beneath the muscularis mucosa are evidently at times in the dilated lymphatics described above.

2. Along the borders of the blood-vessels of the submucosa, having a similar band-like formation, and being most numerous along the border of the vessel nearest to the mucosa.

3. At the junction of the longitudinal and circular muscular coats, in the form of a loose network.

The bacilli are found scattered through the circular muscular coat in fair numbers, often in quite large masses between the muscle fibres, and in these instances in the same areas where the polynuclears are abundant. The longitudinal muscular coat and the peritoneal exudate show a few bacilli, usually singly or in twos and threes.

#### REMARKS.

Clinically the case presents no very striking features. The œdematous form of anthrax is certainly rare in this country, but numerous cases have been reported elsewhere. That the infection took the œdematous form was probably due to its location, most cases of this variety occurring about the eyelids, presumably on account of the thinness of the skin and the loose character of the cellular tissue in this region.

Debron' reported a very similar case in 1865, though in his case the intestinal lesions were not so far advanced as in ours, and there was no endocarditis present.

The occurrence of clinical symptoms, pointing to peritonitis and intestinal lesions, is worthy of note, as in a number of cases with extensive intestinal involvement no local symptoms at all were present.

Mahomed<sup>4</sup> and Haase<sup>3</sup> report such cases, whilst Verneuil<sup>4</sup> and Houel,<sup>5</sup> on the other hand, report cases similar to ours, with well marked abdominal symptoms.

The presence of abdominal symptoms may be of value in pointing out beginning intestinal involvement, as in a recent and interesting case reported by Schütte,<sup>6</sup> in which there were independent infections of the skin and intestinal tract at quite long intervals.

Schütte's case also illustrates the differences between primary and metastatic anthrax.

The patient was a butcher's apprentice, who assisted in killing a cow affected with anthrax.

Five days later there appeared on the upper lid of the right eye a carbuncle, the patient not complaining of abdominal symptoms until fourteen days afterwards.

At this time he had pain in the abdomen, constipation having preceded the pain for several days.

Death occurred on the 16th day after infection. Already at this time the malignant pustule had begun to disappear, but there was an extensive œdema over the face and neck, as well as of the mucous membrane at the entrance to the epiglottis. Moreover there was a typical anthrax "mycosis intestinalis," with hemorrhagic lymphadenitis of the mesenteric and retro-peritoneal lymph glands.

Although the spleen was not inconsiderably enlarged, anthrax bacilli could not be found, either in it or in the œdematous skin of the neck, neither could they be found in the neighborhood of the pustule, which was opened four hours post mortem; but streptococci and staphylococci were cultivated from the bloody fluid.

From the mesenteric lymph glands, in addition to colon bacilli, and streptococci, anthrax bacilli showing great virulence for mice were cultivated. These latter were found in large numbers in the pathological lesions in the stomach and intestines, where they occurred especially thickly, and at the inner margin of the necrotic tissues, becoming progressively fewer as the deeper layers were reached.

They were never found in the blood-vessels, though in these there were many streptococci, these being especially numerous in the spleen.

In this case we have to deal with a primary carbuncle of the skin, and also a primary intestinal infection. From the latter situation the lymph glands became infected through the lymphatics. Upon these first infections there was added later a general streptococcus infection through the blood current. How did the intestinal infection occur?

It could not have occurred at the same time as the skin infection, inasmuch as fourteen days elapsed between the two. It could then only have occurred either in consequence of the scratching of the itching pustule by the patient himself (in which pustule, during life, anthrax bacilli had been demonstrated), the bacilli having thus been carried to the mouth; or the original blood had become dried on his hands or some other part, and the spores had been carried by himself into the intestinal canal.

Our case evidently differed entirely from this, the intestinal affection being secondary to the local one, and taking place through the blood current; the clinical symptoms show that the intestinal lesions occurred within a day or two of the original lesion, and the pathological findings leave no doubt as to the part played by the blood-vessels.

The case is interesting from a pathological point of view on account of the endocarditis, the peritonitis, and the intestinal lesions.

Endocarditis due to the bacillus anthracis appears to be rare; we have only been able to find two cases reported, both of them by Eppinger.<sup>7</sup>

Our case differs from both of Eppinger's, in that we found a perfectly fresh endocarditis on a previously normal valve, whilst in both of his cases, though there was a fresh endocarditis, there was also evidence of old valvular disease, the latter of course probably not due to the anthrax bacillus. The fresh vegetations in Eppinger's cases, and ours, were, judging from his description, of similar formation, though apparently the anthrax bacilli were present in much smaller numbers in his cases.

In one of his cases the evidence goes to show that the endocardial infection was not conveyed, at any rate not entirely, by the heart's blood, but took place by means of infective emboli, occluding the newly formed vessels in the chronically diseased valve. As Eppinger points out, this process could not occur in a normal valve, which is free from blood-vessels, and was only possible on account of the pathological vascularization brought about by the old endocarditis.

Actual peritonitis due to the anthrax bacillus would also seem to be rare.

In the cases of Mahomed,<sup>2</sup> Houel, and Waldeyer,<sup>8</sup> the peritoneal cavity contained large quantities of fluid of a serous character, but in none of these cases was fibrin present, though in Waldeyer's case the visceral peritoneum was injected and slightly cloudy. In none of the cases were the microscopical characters of the fluid ascertained.

In Krumbolz's<sup>9</sup> case fluid was also present, and though its microscopical characters are not mentioned, the anthrax bacillus was found in it, both in cover-slip and culture. It is quite possible that cultures and cover-slips would have shown the bacillus in all these cases, for in our case the fluid did not at all resemble pus, nor the ordinary serous peritoneal exudate, whilst the description of the fluid in the cases above mentioned would lead us to believe that it was probably similar in character.

The intestinal lesions found in our case correspond very accurately, as far as the gross appearances are concerned, with those described by v. Recklinghausen,<sup>10</sup> v. Wahl,<sup>11</sup> Baumgarten<sup>12</sup> and others. We have been unable to find any minute microscopical description of these lesions, though in general characteristics the lesions seem to have corresponded fairly well with ours.

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