REMARKS

ON

A COCCUS PATHOGENIC TO MAN AND ANIMALS: STAPHYLOCOCCUS HÆMORRHAGICUS.

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DR. JAMES G. E. COLBY, of Malton, in Yorkshire, informed me some time ago that within a short time he had seen three cases of a vesicular eruption on the hand of patients who some days previously had been skinning sheep spontaneously dead from "gargle" a few days after lambing. Dr. Colby further informed me that "other medical men of his district had seen similar cases of the vesicular eruption in this and other years." At my request Dr. Colby sent me in glass capillary tubes a little of the lymph withdrawn under proper precautions from the vesicle of the last patient, and this lymph was subjected to bacterioscopic investigation, the result of which I here propose to describe. Before doing so I will give Dr. Colby's account of three cases of vesicular eruption in man in his own words.

The patients all came in from farms on the wolds not less than seven miles away, and opportunity for observation was limited.

CASE I.—May 18th. M. R., farmer, complains of a swelling on his left hand, which first came on as a pimple about two weeks ago, and has gradually enlarged. Thinks he got it from a sheep that died a few days after having lambs and that was attended to and subsequently skinned by him. Feels well in himself. On the left hand, over the head of the fourth and fifth metacarpal bones and base of the proximal phalanges, is a large flat bulla which has already ruptured, and is exuding a thin fluid which is becoming turbid. The skin of the bulla is opaque and thick, and is separated from the tissues beneath by a network of thickened trabeculae containing the fluid. The surrounding skin is red, and the cubital gland is enlarged and tender. There is no rise of temperature. The whole soon healed after treatment.

CASE II.—May 23rd. W. T., 56, shepherd, presents a swelling on the left wrist, and gives the history that it first came as a pimple on May 10th, that on May 16th he pricked it and let out clear blood. Since May 20th blebs have come out round it. Feels quite well. Now, situate over the left wrist is a flattened vesicle 23 mm. to 26 mm. in breadth, with a slightly depressed cicatricial centre and lobulated circumference. The elevated skin is firm and thick, and surrounding tissues are red and puffy. The axillary glands are enlarged, and the temperature is 99° F. He says that on April 19th he skinned a sheep that died of "gargle." Healing was slow but complete.

CASE III.—B. P., farmer, aged 26. Has a swelling on the right hand which was very small when first noticed, but has since enlarged, till now it is 10 mm. by 9 mm. Does not know how he got it, but on questioning says that thirteen or twenty-one days ago he skinned a sheep that died after having three lambs, two of which were born dead. The sheep refused food, wasted, and died in three days. He skinned it two days after death. During the season he lost eight or nine in the same way. He now presents on the back of the second metacarpal bone a well-defined flat vesicle, bluish-grey in colour, and with a slightly depressed centre. He has no pain, and there is little surrounding redness, but the axillary glands are enlarged. The temperature is normal. Fluid was collected in capillary tubes, and forwarded to Dr. Klein; after which it was removed by scraping, and a solution of corrosive sublimate applied.

June 16th. Some erythematous rash on the hands and feet; wound looks well, and there is no apparent constitutional disturbance.

June 17th. Erythema still to be made out.

June 28th. Wound heals slowly.

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Single cases of this affection in man have occurred in previous years, and been attributed to various causes, but the connection of these three with diseased sheep is quite clear. The appearance of the lesion in Case II suggested to others that it was anthrax, and the resemblance was close, but differed chiefly in the absence of necrosis. In sheep the disease locally known as "gargle" appears to be confined to the lambing season, and to ewes which have recently had lambs, though it is said to occur after shearing. It is very easily conveyed from one to another, runs a course like puerperal fever, and is very fatal, the majority dying in three to six days. In some the vulva and vagina are said to become black and occasionally the udder to be swollen, but there is reason to believe that more than one disease is included under the term.

The fluid sent in the capillary tubes by Dr. Colby was of a sanguineous-serous character. Examined under the micro-

scope it contained numerous red blood corpuscles and leucocytes and cocci, the latter as dumb bells, but chiefly as small masses. The cocci measured 0.4 to 0.6 μ in diameter, some showing the division into two crescentic granules, common amongst staphylococci.

Plate cultures on the surface of nutrient agar and nutrient gelatine were made by rubbing a droplet of the fluid over the surface of the set agar and set gelatine, incubating the former at 37° C., the latter at 20 to 21° C. In these plates an abundance of colonies came up. In one agar plate I counted over a hundred colonies; in the other agar plate their number in one part of the plate was so great that they were closely placed and uncountable. In the four plates that were made (two agar and two gelatine) I could discover only three colonies which were those of the common staphylococcus pyogenes albus; all the others were of a different kind, but possessed of the same characters.

The characters of these colonies in the plates and in the subcultures made from them in the different media are briefly as follows: On agar the colonies after twenty-four hours are round, moist, flat, white in reflected brown in transmitted light, only slightly raised above the surface; under a magnifying glass they look granular, thickest in the central part, and possessed of a narrow filmy margin. They grow rapidly in size, and reach in several days a diameter of from 0.2 to 0.5 centimetres, at the same time the marginal filmy zone becoming more pronounced; after about a week each colony possesses over the greater part of its circumference a filmy, more translucent, marginal zone, somewhat irregular in outline and radially striated, the middle part being granular and of a somewhat concentric arrangement. In reflected light the colony already after a few days assumes a light yellowish colour, which, however, never becomes deep, and this colour is observed only on the larger colonies.

On gelatine plates the colonies are noticed already after twenty-four hours under a magnifying glass as minute grey round dots, which show a dark centre and a more translucent margin. After two to three days the colony, while enlarging, commences to sink into a pit in the gelatine, owing to liquefaction; this liquefaction proceeds slowly and gradually, leads to the formation of a circular area of slightly turbid liquefied gelatine, in the centre of which is the whitish mass of the main colony.

In agar streak culture the growth forms a gradually broadening flat band, thicker in the middle, thinner in the peripheral part, the margin of this latter irregularly outlined. The streak is white in reflected light, after some days it assumes a yellowish tinge.

In gelatine streak culture the band of the growth liquefies the gelatine and sinks under the surface; as the liquefaction proceeds it forms at the bottom of the liquefied gelatine a whitish powdery mass, which after ten to fourteen days assumes a yellowish tint. The liquefied gelatine is slightly turbid.

In gelatine stab culture the line of inoculation is indicated after twenty-four to forty-eight hours by a linear mass composed of spherical droplets, white in reflected, brown in transmitted light; on the upper free end of the stab there is a whitish plate-like expansion of the growth. Liquefaction commences at the upper free end of the stab after two to three days, the top plate of the growth sinking in; the liquefaction proceeds slowly, so that even after ten to fourteen days it has not reached more than a third or a fourth of the growth, forming in the upper part of the culture a funnel-shaped turbid liquefied mass.

In alkaline broth at 37° C. the microbe grows rapidly, causing already in twenty-four hours turbidity; in alkaline litmus broth the growth is also good; after a day or two the litmus commences to change into neutral, and after two to four days into acid (red).

In milk at 37° C. the microbe grows well; during the first five to seven days the milk remains fluid, but after seven or eight days it thickens and a separation into turbid whey and casein coagula sets in; this separation is complete after nine or ten days.

On steamed potato at 37° C. the microbe forms a transparent film which gradually thickens in the marginal part; at first it is greyish, and later on assumes a yellowish tinge in the thicker marginal part.

On solidified blood serum at 37° C. a greyish filmy growth appears already after twenty-four hours, this thickens, and after three to four days assumes a yellowish tinge in the thicker marginal part. No liquefaction of the serum is noticed at any time. The microbe dies when exposed to a temperature of 62° C. for five minutes.

From these characters it appears that we have to deal with a coccus which belongs to the tribe of staphylococcus, more particularly to that group which comprises the staphylococcus pyogenes aureus.

Nocard described¹ a coccus, isolated by him from the milk gland in gangrenous mastitis of sheep (*mal de pis, araigné*), with the culture of which he produced by injection into the milk gland of healthy sheep the same disease and death. The coccus which we isolated from the fluid of the vesicle on the hand of man is closely related to the micrococcus of Nocard, but differs from it in the following respects: (a) Nocard's coccus liquefies gelatine in stab conspicuously faster than does our coccus; (b) Nocard's coccus coagulates milk into a solid mass already within twenty-four hours, our coccus does not coagulate milk before five to seven days, and does not do it in the same way, for the curdling consists in a separation of turbid whey and coagula of casein; (c) Nocard's coccus liquefies solidified blood serum, our coccus does not liquefy blood serum at any time.

Of greater importance, however, and indicating a more profound distinction between Nocard's and our coccus are the following facts:

1. The coccus of Nocard is found associated with, and causing, gangrenous mastitis in milch sheep; our coccus was isolated from a vesicle on the hand of a man who had skinned a sheep that had died, not from gangrenous or any other mastitis, but soon after lambing.

2. The gangrenous mastitis (*mal de pis, araigné*) in milch sheep has, according to Nocard and his informants,² a considerable distribution in some districts in France, where the milk of sheep is used for making Roquefort; yet there is nowhere any mention made of a cutaneous infection of human beings. If the two diseases in the sheep—namely, gangrenous mastitis (or *araigné*) and the puerperal disease from which the Malton sheep died—were the same, and the two microbes identical, such a cutaneous infection of human beings as occurred in Malton could not have been wanting in France, considering the number of sheep affected with *araigné*, and the number of men attending to their milking.

3. A striking difference between the two microbes is, however, shown by the behaviour of their cultures on guinea-pigs. Nocard's coccus injected subcutaneously into guinea-pigs, even in large doses of otherwise virulent culture, produced at the utmost a rapidly passing local swelling; in the rabbit large doses produced swelling and local abscesses³; cultures of our coccus on the other hand, prove very virulent for the guinea-pig. A small dose of a serum culture, a moderate dose of a gelatine, or recent agar culture; for example, a few drops of the turbid condensation water in a serum culture, 1 to 2 platinum loops of a gelatine culture several days to several weeks old, 1 to 2 loops of an agar surface culture twenty-four hours to four days old, when subcutaneously injected into the groin of a guinea-pig of 200 to 300 grammes body weight, causes already after twelve hours hæmorrhagic œdema in the subcutaneous and muscular tissues, extending rapidly over the inside of the thigh, groin, abdominal, and thoracic walls, and even into the neck; death according to the virulence of the culture takes place in from twenty to sixty hours. Serum cultures act most virulently, causing death in twenty hours. Gelatine cultures stand next in virulence. Agar cultures prove virulent up to the fourth or fifth day, later than this the virulence diminishes considerably, causing a circumscribed hæmorrhagic œdema, but the animal recovers. After a week, agar culture does not produce even local hæmorrhagic œdema. Broth cultures behave in a similar way. When quite recent they prove virulent; after six or seven days their virulence is greatly diminished. The virulence can be re-established by transference to serum cultures, or gelatine or agar cultures.

When the animals die, the following condition is found on *post-mortem* examination: the subcutaneous and subjacent muscular tissues of the thigh, groin, abdomen, chest, and even neck are much swollen, containing a considerable

amount of sanguineous serous fluid; there is no gas and no odour. The liver is pale and small, the spleen and lungs are not abnormal; the peritoneum and serous covering of the intestine are in a percentage of cases greatly injected, and the peritoneal cavity in these cases contains sanguineous fluid. The subcutaneous exudation shows under the microscope numerous red blood corpuscles and leucocytes, an abundance of cocci as single cocci, as diplococci, and as small masses. The protoplasm of the leucocytes is densely filled with the cocci. The peritoneal exudation, when present, possesses the same characters. Cultures made of the subcutaneous fluid yield pure cultures of our coccus, so does the peritoneal fluid; the heart's blood yields on culture only a limited number of colonies, a loop of blood yields between 10 and 15 colonies only. Intraperitoneal injection of a small dose (1 to 2 loops) causes death from intensive peritonitis already in six to ten hours. The peritoneal cavity contains copious sanguineous fluid, in which are seen red blood corpuscles and numerous leucocytes; the protoplasm of the latter is densely filled with the cocci; the fluid part contains the cocci also in great abundance.

Very small doses of virulent, or larger doses of attenuated, culture cause on subcutaneous injection general illness, passing off after two or three days, with local œdema, which after several days disappears. Such animals acquire hereby a certain, though not a very high resistance against large doses of virulent culture.

In the rabbit the result after subcutaneous injection is this: general illness and extensive hæmorrhagic œdema, which leads to necrosis of the skin over the abdomen. Death takes place from general marasmus in about three weeks.

Owing to the lambing being over at the time when the above investigation was commenced, no further cases of sheep dying after lambing were available, and therefore the investigation of such sheep has to be postponed till the spring of next year; but I have inoculated healthy sheep with virulent gelatine culture of our coccus, a sixth subculture being used for the purpose.

Two healthy sheep were injected subcutaneously into the thigh with a bouillon suspension of a gelatine culture, about one-fourth of a culture being used for each animal. Next day both animals were found ill; the temperature was raised (104° F.), and the animals did not feed; the leg of the injected side was swollen and retracted, the swelling extending over the whole leg and the groin, and the skin being dark red and hot to the touch; the muscle and subcutaneous tissue puffy. The animals could not stand or walk.

On the third day the condition was much worse, both as regards the general state as also that of the injected leg. Temperature 105.8° in the morning, 106.2° in the evening, breathing very rapid. At the end of three days one animal was found moribund; it was killed, and on *post-mortem* examination the following condition was found: The skin of the groin and thigh of the injected side dark red; on cutting into it and exposing the subcutaneous and muscular tissues extensive œdematous hæmorrhagic swelling of both tissues is found, with copious sanguineous serous fluid. Under the microscope this fluid contains numerous red and white blood corpuscles and cocci in clusters and as dumb-bells.

No growth of cocci or any other microbes was obtained by culture from the heart's blood, but cultivation in the plate and in tubes with a trace of the subcutaneous fluid yielded innumerable colonies of the cocci, which on subculture proved exactly the same as were used for the injection. No disease of the viscera could be found.

With a loopful of the growth of the sheep's exudation on the surface of agar after twenty-four hours' incubation at 37° C. a guinea-pig was injected subcutaneously. The animal died in twenty hours with exactly the same appearances of extensive hæmorrhagic œdema as were described above.

On account of the effects produced in the guinea-pig and sheep after subcutaneous injection, I propose calling the microbe staphylococcus hæmorrhagicus.

With the same agar culture, namely, that obtained from the sanguineous exudation of the above sheep, and which proved virulent for the guinea-pig, I inoculated in five simple punctures the skin on the dorsum of my own left hand. Next day all the punctures were raised and surrounded by an

areola; there was rather an unpleasant itching, but I felt in no way ill, and the temperature was normal. After forty-eight hours the punctures had somewhat further advanced, each puncture being a fairly distinct papule surrounded by a spreading areola; the itching was now rather troublesome; the general condition and body temperature were normal. After seventy-two hours in two of the punctures the papules were well raised, and in their centre was distinct accumulation of congealed serum; the other three punctures, though pronounced papules, were not so well raised, but in all five punctures the areola was well marked. General condition and temperature normal. Local itching rather troublesome. After four days in two of the papules distinct accumulation of pus in the depth could be made out; in all punctures the superficial part commences to scab; the areola is still pronounced, but a little less broad than on the previous day; the elbow pit a little painful, and its glands just to be felt. General condition normal. After five days same condition. Areola receding; no pain or swelling in the elbow pit. After six days scabs on all punctures distinct, areola only indicated.

By the tenth day the scab and superficial epidermis over the original areola desquamating. By the sixteenth day only two of the punctures still show traces of desquamation, the other three are just indicated as dark spots.

On the sixth day I got out from one of the pustules a little purulent matter; on examining it under the microscope and in culture our staphylococcus was found in abundance.

The inoculation with agar culture in our case was, therefore, by no means so pronounced as in the case of the natural infection of Dr. Colby's patients, but it was sufficiently well marked to indicate a positive result.

In conclusion, I wish to mention the fate of the second inoculated sheep. This animal remained very ill for ten days; it could not stand or walk, its temperature remaining high, being 105° morning and 105.6° in the evening; the animal drank a lot of water, but, although fed by the attendant, consumed very little food. With the third week it began to mend in a decided way, the temperature falling to 104° or 104.6° respectively; and the skin of the thigh becoming necrotic, the animal could and did walk, though it did not use the leg of the injected side. By the end of four weeks its temperature was still 104°, the injected leg not being used for walking; the animal fed fairly well, but was extremely emaciated.

REFERENCES.

- ¹ *Ann. de l'Inst. Pasteur*, vol. 1, 1887, pp. 417-428. ² *Loc. cit.*, p. 418. ³ *Loc. cit.*, p. 426.

FINAL REPORT OF A CASE OF A VERY LARGE INNOMINATE ANEURYSM

COMPLETELY CURED BY THE EMPLOYMENT OF ELECTROLYSIS THROUGH TEN FEET OF SNARLED, COILED, FINE GOLD WIRE, INTRODUCED INTO THE SAC; DEATH AT THE EXPIRATION OF THREE AND A HALF YEARS FROM CEREBRAL THROMBOSIS.*

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It has recently been the writer's extreme good fortune to obtain a necropsy on the case of a very large innominate aneurysm on which he, over forty-one months before, employed galvanism through ten feet of coiled gold wire, which he had introduced, resulting in complete solidification of the sac. The history of this case was published in detail in the *American Journal of the Medical Sciences* very recently (August, 1896), so need not be repeated here. Suffice to state that the case was one most unpropitious for any treatment. The patient was what in street parlance is styled a "bum" or "rounder," who had been a habitual spirit drinker. He was also a syphilitic, had pronounced aortic and mitral disease, with extensive cardiac enlargement, generalised endarteritis, and had also chronic nephritis. The aneurysm formed a large and prominent swelling at the roof of the neck. It was

regarded as springing from and being limited to the innominate artery. The sac wall was of extreme thinness, and, at least externally, was unprotected by clot. This, which was apparent to the eye and touch, was further demonstrated by puncture with needles. At the time of operation the sac wall seemed on the point of bursting externally in several situations over which the skin was extremely thin and bluish.

The result of electrolysis through the introduced wire was very decided. Clot formation, leading apparently to solidification of the sac, was early manifest. The patient lived for nearly three years and a half after operation, and finally died as the result of the formation of a large thrombus in the middle cerebral artery, the result of the advanced endarteritis present. Despite the most unfavourable condition of the patient, his bad cardiac and renal disease and generalised arterial sclerosis, his having had syphilis, and being a steady spirit drinker, the result obtained, which I show you to-night, speaks strikingly in favour of this procedure as a method of treating sacculated aneurysm. The sac has been found to be of extreme hardness, with complete consolidation and obliteration of its cavity.

Report of the Necropsy.—G. D., aged 43, white, male, died December, 1896. Necropsy made by Dr. A. A. Chriskey and the writer four hours after death. Body fairly well nourished. Aneurysm tumour noted in the situation described. Thorax: The solidified tumour with clavicle and three ribs on the right were removed, and the thoracic cavity exposed. The clavicle with the three ribs, the ascending and descending aorta, heart, and pericardium removed *en masse*. Lungs: Slightly adherent at both apices. The bases showed hypostatic congestion. Abdominal cavity: The spleen was somewhat enlarged; its section showed it to be intensely congested, with the trabeculae visible. Stomach normal in size and situation. Small and large intestines normal. But one kidney could be found; this was considerably enlarged. It was thought to have been placed aside with the other specimens for subsequent examination, but unfortunately must have been returned to the body, as it afterwards could not be found with the specimens. The liver was somewhat enlarged, and deeply congested. The gall bladder contained fluid bile; the common bile ducts were patulous. Heart: Pericardium non-adherent. The sac contained a normal quantity of fluid. The heart was very much enlarged, 26.5 cm. in circumference. Length of the interior left ventricle 11 cm. Thickness of left ventricular wall, 2.5 cm.; thickness of right ventricular wall, 1.2 cm. The cardiac muscle was of dark red colour. No areas of opacity apparent. Aortic leaflets thickened. Above their inferior attachment for a distance of 1 cm. the leaflets were densely sclerosed. The aortic valve was found to be very insufficient. Superior borders of two of the leaflets were densely sclerosed. A few atheromatous patches were present on the intraventricular surface of the aortic valves. The mitral valve was very patulous, thickened, and slightly opaque, and markedly insufficient. Left auricle was dilated with thickened walls. Right auricle was normal in size; tricuspid and pulmonary valves were normal. The coronary arteries were patulous. The aorta from its origin is the seat of very diffuse atheromatous degeneration with small areas of calcification. Internal circumference of the aorta above aortic valves 10 cm. The aorta was dilated from its cardiac origin, but a separate and very distinctly outlined extensive fusiform dilatation existed from 13 cm. to the left from the origin of the left subclavian artery, at the junction of the transverse with the descending portion of the aorta, downward to a distance of 10 cm. This fusiform sac at its greatest internal circumference is 15 cm. This dilatation—a typical fusiform aneurysm—is sharply defined above and below by concentric elevated rings or constrictions of the whole circumference of the aorta. The entire aorta, including the dilated portion, is uniformly thickened. The inner surface of the fusiform sac shows widespread atheromatous patches. The sacculated aneurysm springs directly from the root of the innominate artery. The aneurysmal sac is approximately the size of a foetal head at term; length, 13 cm.; transverse diameter, 9 cm. The sac is completely consolidated with organised coagula in which lie the coils of wire. The consolidated sac has at its base a small *cul-de-sac*, the remains of the innominate artery. This, from the aorta, admits the little finger to a distance of 4 cm. through an annular ring, sharply defined, 2 cm. in diameter. The *cul-de-sac* was noted to contain in its interior a small coagulum, presumably of *post-mortem* formation. The sac itself was very firm and wholly solidified, and when cut into was found to be completely occupied by organised material, in the interstices of which lay the coils of fine gold wire. Brain: A large thrombus is evident in the left middle cerebral artery. Softening has occurred in the region of the corpus callosum, caudate, and lenticular nucleus, and in the internal capsule of the left side.

The writer has now treated two cases of sacculated aneurysm by the employment of electrolysis through introduced wire, and has directed the technique in a third successful case. This has naturally led him to give a good deal of attention to the subject. The result in his second successful case, the necropsy of which is here reported, and that obtained in the case treated by Dr. Hershey, of Colorado, in which the solidification of the aneurysm resulted by this method,¹ is sufficiently suggestive to engage the attention of the therapist.

The history of the treatment of aneurysm by this method need not here be entered into, it having been thoroughly reviewed by the writer in his initial paper on the subject,² and

* Read before the College of Physicians of Philadelphia.