(h) The results obtained in these series were most unsatisfactory and were at complete variance with those reported in the preliminary account of the use of this preparation.

Conclusions

1. The serum described as "gonococcal antitoxin" appears to have no specific anti-gonococcal effect.
2. It appears to delay the development of the active immunity essential to recovery from gonorrhoea without substituting any compensatory passive immunity.
3. Its use in gonorrhoea is inadvisable on account of its lack of therapeutic value, its serious side-effects, its frequent interference with recovery, and possibly also the risk of its rendering patients liable to suffer from serious allergic reactions in the event of their requiring at some future date treatment with antitoxic sera for other bacterial infections.

[In a communication published after this paper was written Anwyl-Davies (*St. Thomas's Hospital Reports*, 1937, 2, 67) states that since his first report appeared many additional patients have been treated with an improved unconcentrated antitoxin. The precise number of patients is not stated, but the results claimed are: "excellent" and "good" together, 78 per cent.; "fair," 18 per cent.; "bad," 4 per cent.; with no clinical relapses to date.]

The London County Council accepts no responsibility for the opinions or conclusions expressed in this article.

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A HUMAN INFECTION WITH ACTINOMYCES CAPRAE

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The subject from whom this organism was isolated was one of two cases (Case I) of acholuric jaundice in a brother and sister. The following are the clinical histories.

Case I

A girl aged 14 was admitted to hospital on May 22, 1936, with a diagnosis of acholuric jaundice and splenomegaly. Her father was alive and well, with no history of jaundice and no evidence of jaundice or splenomegaly when he was examined on June 6, 1936. Her mother was healthy and active and without jaundice. One brother (Case II) had jaundice and splenomegaly. Four other children were alive and well.

Clinical History.—The patient was healthy at birth, but developed jaundice, which persisted. She had measles when a small child, and while in hospital in 1930 she contracted diphtheria. She was sent to the fever hospital and recovered without complication. The patient suffered from attacks of abdominal pain, mainly on the left side, associated with vomiting and a cold in the head. These attacks occurred every two or three months. The yellow colour increased with the attacks of vomiting. The motions had been normal in colour and the urine had not been dark.

Examination.—The patient was seen to have an adenoid facies and a marked icteric tinge of the skin and conjunctivae. There were petechial haemorrhages on the arms and trunk. Her weight was 74 lb. (the average for 11½ years). The right tonsil was larger than the left, and her teeth were normal. No abnormality was found in the heart and lungs. The spleen was greatly enlarged, and extended to one inch below and two inches to the right of the umbilicus. It was firm and not tender. The liver was slightly enlarged. There were no enlarged lymph glands. The urine was dark; bile was not present, but the test for urobilin was positive, and albumin was found. The deposit showed numerous cellular casts but no organisms. A blood count showed: red cells, 2,280,000 per c.mm.; haemoglobin, 46 per cent.; colour index, 1.0; white cells, 7,200 per c.mm. Differential count: polymorphs, 64 per cent.; lymphocytes, 22 per cent.; mononuclears, 6 per cent.; eosinophils, 8 per cent. All the red corpuscles were small, and two nucleated red cells were seen. There was some anisocytosis, poikilocytosis, and punctate basophilia, and platelets were present. The van den Bergh reaction (indirect) was positive. The icteric index was 55, the bleeding time two and a half minutes, and the coagulation time eight minutes. In the test for fragility haemolysis began at 0.66 and was complete at 0.54 per cent. (a normal control began at 0.32 and was complete at 0.28 per cent.). The sigma reaction was negative. Blood group, IV. An x-ray report on the hands showed no signs of rickets, but there was slight osteoporosis of the metacarpals. The patient was kept under observation in hospital for a month and was given large doses of potassium iodide, but no change occurred in the size of the spleen.

Operation.—This was performed by one of us (R. H. R.-I.) under gas-and-oxygen anaesthesia (Dr. Duigan). The spleen was exposed by a V-shaped incision. The head of the pancreas was found to be closely adherent to the pedicle of the spleen. There were some adhesions, which were ligatured, between the spleen and the stomach and kidney. The pedicle was carefully divided and the spleen removed without any excess of bleeding. The wound was closed with silk-worm-gut sutures to the skin surface.

Progress.—The jaundice disappeared within a week and recovery was uneventful. The patient was discharged to a convalescent home on July 27, 1936. In October, 1937, she had grown and put on weight, and was more normal in appearance, without jaundice, though the tonsils were very large. A blood count showed: red cells, 4,990,000 per c.mm.; haemoglobin, 90 per cent.; colour index, 0.9; white cells, 17,000; reticulocytes, 0.07 per cent. The differential percentages were: eosinophils, 4.5; metamyelocytes, 1.5; neutrophils, 55.5; large lymphocytes, 2; small lymphocytes, 35.5; monocytes, 2.5. In the film there was slight anisocytosis, and most of the red corpuscles appeared smaller than normal. Poikilocytosis was slight, and no polychromasia, punctate basophilia, or nucleated forms were present. The fragility began at 0.4 per cent. and was complete at 0.32 per cent.—less than before operation and only slightly above a normal control.

Case II

A boy aged 7, brother of Case I, was admitted to hospital on May 22, 1936, with a diagnosis of acholuric jaundice and splenomegaly. He had been a full-time normal baby, weighing 8 lb., and was breast-fed. Jaundice persisted from birth, and he also had measles when 4 years old. He was always tired. The jaundice varied somewhat, and he had frequent attacks of sickness with pain in the abdomen, sometimes being constipated. The stools were normal in colour.

Examination.—He had an adenoid facies, with an appearance of having a large head; measurement, however, gave a circumference of 20½ inches (normal for age). His weight was 49½ lb. His intelligence was rather below the average. There was general slight jaundice, which included the conjunctivae. Petechial haemorrhages appeared on arms, legs, abdomen, and chest. The left tonsil was larger than the right. The upper and lower central incisors were notched along the cutting edge, but there was no suggestion of

syphilis. No enlarged glands were observed, and the thoracic organs were normal. The spleen was enlarged to half an inch below the level of the umbilicus and as far as the mid-line, while the liver edge was palpable below the costal margin. The urine was clear, natural in colour, and contained no bile, but urobilin was present in small amount. There was no deposit. The blood count was as follows: red cells, 4,230,000 per c.mm.; haemoglobin, 64 per cent.; colour index, 0.7; white cells, 9,500. The differential count showed: polymorphs, 28 per cent.; lymphocytes, 62 per cent.; monocytes, 10 per cent. The red blood corpuscles were small, there was marked punctate basophilia and polychromasia; platelets were present but not abundant. The icteric index was 32 units. The Wassermann and sigma reactions were negative. Fragility of the red cells began at 0.6 per cent. saline and was complete at 0.32 per cent. A normal control done at the same time began at 0.32 per cent. and was complete at 0.28 per cent. Under observation the spleen became very slightly smaller and the jaundice less marked.

Operation.—This was performed by one of us (R. H. R.-I.) on July 6, 1936, under gas-and-oxygen anaesthesia given by Drs. Duigan and Alsop. The abdomen was opened by a V-shaped incision; the spleen was very large, and was adherent to the stomach and kidney, the hilum being closely involved with the tail of the pancreas. The adhesions were divided, the pedicle ligatured and divided, and the spleen removed without loss of blood. The wound was closed and strengthened with silkworm-gut sutures. The wound healed well and the jaundice disappeared after the third day. The patient was discharged on August 1, 1936.

In October, 1937, he was a well-nourished boy without jaundice, and on examination his blood count was as follows: red cells, 5,020,000 per c.mm.; haemoglobin, 94 per cent.; colour index, 0.94; white cells, 18,800 per c.mm.; reticulocytes, 0.2 per cent. The differential count gave the following percentages: eosinophils, 4; metamyelocytes, 0.5; neutrophils, 62.5; lymphocytes, 29.5; monocytes, 3.5. The film showed slight anisocytosis and poikilocytosis; the corpuscles were small, but no polychromasia or punctate basophilia was present. The fragility was less than before the operation, but was not normal.

Description of the Spleens

Case I.—The organ was about five times the normal size and weighed 1,314 grammes. It had shrunk considerably from loss of blood. The substance was firm and was deep red on section; the capsule was slightly thickened. Malpighian bodies were difficult to identify, but trabeculae were easily seen, and some of them showed reddish opaque points of the siderotic or Gandy-Gamna nodule. Histologically several of these showed thick mycelial fibres, some undergoing calcification. In a few instances these fibres appeared to be in process of absorption. Eosinophils were present everywhere in the splenic tissue. It was possible to excise thirty-six of these nodules under aseptic precautions. They were ground up with a little broth in a sterile mortar and inoculated upon twenty-four whooping-cough agar plates and a dozen tubes of the same medium. After a week one plate suggested a growth of actinomyces, and after four weeks the greater part of the surface was spread over with an actinomyces growth, salmon pink in colour and adherent to the underlying medium. The plates otherwise were sterile except for a few colonies derived from air contaminations.

Case II.—The organ preserved its shape and was three times the normal size—8 in. by 4 in. by 3 in. The capsule was turgid but not thickened. Numerous minute buff-coloured siderotic (Gandy-Gamna) nodules could be identified in each cross-section of the spleen. The pulp was congested and moderately firm. Malpighian bodies could be distinguished only with difficulty. As in Case I

the procedure was adopted of grinding up a number of excised nodules in broth. Altogether the inoculations were made on fifty-one tubes of various media, solid and liquid, and eleven whooping-cough plates. Except for a few obvious contaminations these proved sterile, observed during a period of several months.

Description of the Organism

Subculture on broth after one week's incubation at 37° C. showed small flocculent colonies at the bottom of the tube. On the surface of the broth was a pellicle composed of small spherical orange colonies covered with a layer of white aerial mycelium. The appearance so strikingly resembled that of a strain of *Actinomyces caprae* obtained from the national collection of type cultures that parallel series of cultures of both organisms were made on whooping-cough agar (as used in the Serum Institute at Copenhagen), litmus milk, Dorset's egg medium, and blood agar, on which *Actinomyces caprae* shows its most characteristic features. Both organisms presented identical appearances, as follows: on whooping-cough agar, after seven days' incubation at 37° C., there were numerous orange colonies which had become confluent. The surface was much heaped up, and was covered by a layer of white aerial mycelium. After three weeks the colonies were heaped up still more and the aerial mycelium had turned salmon pink. On litmus milk, after one week at 37° C., the growth on the surface was pale orange. After a month the milk was peptonized. On blood agar, after a week's incubation at 37° C., there appeared small cream-coloured colonies covered by a thick layer of white aerial mycelium. No haemolysis occurred. After one month the colonies had extended so as to produce a thin margin, but there was no haemolysis. On Dorset's egg medium, after a week's incubation at 37° C., there were irregular pimple-like orange colonies covered with a thick layer of aerial mycelium.

Morphologically the strain belongs to Group IIa of Orskov's classification in that after twelve hours at 37° C. the mycelium breaks up into rods and cocci of various sizes and there is early formation of aerial mycelium. The breaking up of the threads begins with the appearance of fine transverse division lines, and the segments which ultimately form are displaced at different angles from one another. The same displacement occurs in the aerial mycelium.

Staining Properties.—The organism is Gram-positive (Claudius's method), and stains readily with haematoxylin, carbol fuchsin, and malachite-green. Parts of the mycelium are acid-fast.

Pathogenicity.—*Actinomyces caprae* is pathogenic for rabbits and guinea-pigs, and Dr. R. L. Vollum kindly undertook to make injections of both strains into these animals. Two guinea-pigs and two rabbits were injected subcutaneously. All the animals killed after three weeks showed subcutaneous abscesses, the strain from Case I producing slightly larger lesions than *Actinomyces caprae*. In all abscesses colonies of actinomyces were found on microscopical section.

Discussion

We are unable to explain the occurrence of *Actinomyces caprae* in the cultures from the excised spleen of Case I except as a pathogenic agent in intimate relation to the splenic tissue. It is inconceivable that it could have been an accidental invasion or contamination. The reason why only one plate was infected is one that concerns the isolation of actinomyces in known cases of this infection:

many specimens have to be taken and but few are positive. The number of cases, however (now amounting to thirteen), from which actinomyces has been obtained from the excised spleen or blood in acholuric jaundice, splenic anaemia, and Banti's disease makes it probable that the present organism bears an aetiological relation to the disease.

This is the first occasion on which a known pathogenic species of actinomyces has been isolated from cases of jaundice. It also appears to be the first occasion on which *Actinomyces caprae* has been found in a human case. *Actinomyces caprae* was first isolated from the lung of a goat by Silberschmidt (1899). Galli-Valerio (1912) obtained it from the same source.

An attempt has been made to identify agglutinin to *Actinomyces caprae* in the blood of the patient. The organism is particularly difficult to emulsify. A thin emulsion, however, made by continual shaking of a twenty-four-hour broth culture showed no agglutination as tested against the serum of Case I. The serum of Case I added to a broth culture of the organism increased the rate of growth and brought out more prominently the characteristic colour of the organism as compared with six normal control sera. Again, the siderotic nodules in the spleen on first exposure were a buff colour, but on being incubated in culture tubes under aerobic conditions they assumed the same tint as an old culture on agar.

The patients come of peasant stock and were born in a cottage which had been part of an old farm; it is said to have been very insanitary, and has since been pulled down. A neighbour used to keep ten to twelve goats, and occasionally these used to stray into the garden of the cottage occupied by the patients. There is no history of their having drunk goats' milk.

Summary

Two cases of acholuric jaundice are described in which splenectomy had the effect of completely relieving the jaundice, restoring the haemoglobin and number of red corpuscles to normal, and diminishing the fragility. From the spleen of one of these patients an organism was isolated which gave the characteristic reactions of *Actinomyces caprae*. It is concluded that this organism was an essential pathogenic agent in the production of the disease.

[Note.—Since the above was written a sister of the patients (aged 17), referred to in the text as normal, has come under observation with jaundice, splenomegaly, and a haemoclastic crisis.]

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On June 16 King Gustaf V of Sweden will celebrate his eightieth birthday, and a national subscription has been opened to celebrate the occasion. In accordance with the King's own desire the funds collected will be used for research into and for combating infantile paralysis and rheumatic diseases. Subscription lists have been issued throughout the country and also in Swedish Legations and Consulates abroad, thus giving an opportunity to Swedes, whether at home or in foreign countries, to contribute. A similar appeal on the occasion of King Gustaf's seventieth birthday brought in the splendid total of just over 5 million kronor (£275,000 at par). The fund on that occasion was earmarked for cancer research and the establishment of cancer clinics. Large sums from this fund have been spent on purchase of radium, and some of the projected clinics have already been opened.

FAMILIAL CLUBBING OF THE FINGERS AND TOES

BY

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Although it is not uncommon to find clubbing of the fingers in the absence of apparent cause (I have seen two instances during the past year), reports of such cases are infrequent, but they have been described by Mangelsdorf (1885), West (1897), and Lewy (1921). Decloux and Lippmann (1902) recorded the occurrence of clubbed fingers and toes in a man aged 55 and in his sister aged 30; there were sixteen other brothers and sisters, who were said to be unaffected, as were their parents and the man's children. None of these was seen. The affected pair said that the condition had been present since birth; neither had any pulmonary or cardiac disease. Weber (1919) put on record the cases of twin brothers aged 25 with clubbed fingers; another brother, aged 30, was not seen, but was said to be likewise affected. All were quite healthy.

Cases occurring in Two Successive Generations

Cases occurring in two successive generations have been recorded in six instances. Fraentzel (1888) described a healthy man showing "drumstick" fingers, his father and his sister having the same condition. Freytag (1891), in his monograph on clubbed fingers, mentioned two instances of father and son being affected in the absence of disease. Weber (1919) found clubbing of the fingers and toes of a man aged 25 and his father; three brothers and a sister had a like condition. Crouzon and Gutmann (1931) reported clubbed fingers in a healthy man aged 30; a radiograph of his hands showed normal bones. The father had been similarly affected, but had suffered from a chronic "broncho-pulmonary" condition. Kayne (1933) published a record of a family in which two brothers, a sister, and the father had clubbed fingers and slightly clubbed toes; the mother and four sisters were normal. The patient's Wassermann reaction was negative, as was a radiograph of his chest. Radiography of his hands showed only slight splaying of the terminal phalanges. In the same year Ragins and Freilich (1933) described a family in which a man, his sister, father, and a paternal uncle all had clubbed fingers and toes.

Witherspoon (1936) reviewed the articles on the subject and reported a negro family in which four brothers and their father had clubbed fingers and toes. One of the brothers had two children, aged 2 months and 17 months, who were found to have pronounced thickening of the volar pads of the fingers and thumbs, but no true clubbing. A maternal half-brother was said to be affected. The mother and four sisters had normal fingers and toes. Wassermann reactions were negative, and radiographs of the chest were normal in all cases examined. Neurath (1932) described four families in which clubbing of the thumbs and big toes was inherited as a simple Mendelian dominant. The clubbing in these cases was due to a bony malformation of the terminal phalanges, and was a special variety of brachyphalangia; for this reason it is not comparable with the present series.

Anomalous Inheritance

In the foregoing reports the inheritance is straightforward, from father to son; but there are two families described in which the inheritance is apparently anomalous.