changes found in these diseases, the anatomical changes may be incurable; but looked at from the standpoint of physiology, the disease is not "incurable"; the course of the disease, the functional efficiency of the patient, is amenable to, often indeed, largely determined by treatment. A patient whose leg had been amputated would not be sent away with the statement that, since it is impossible for him to grow a new leg, nothing can be done for him; by the use of an artificial leg, and by refraining from certain activities, such a patient can become nearly as efficient as a normal man; the same attitude should be taken toward patients with incurable lesions of internal organs; these patients, too, can often be made functionally efficient.

All this bears directly on the question of the correctness of the physiological point of view. Surely this optimistic point of view is a more useful guide, has greater pragmatic value in therapeutics than the pessimistic anatomical point of view. *If usefulness, pragmatic value, are measures of the correctness of a scientific truth, the anatomical point of view is a wrong one from the standpoint of therapeutics and the physiological point of view is the correct one.*

ACUTE ARTHRITIS EXPERIMENTALLY PRODUCED BY INTRAVENOUS INJECTION OF THE STAPHYLOCOCCUS PYOGENES.*

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In a previous paper,† I pointed out that the staphylococcus organism of shifting grades of virulence localized on intravenous inoculation in different structures of the body, and that within certain limits a selective localization of this micro-organism for special organs could be developed by cultivation of the organism in functioning tissue. I also showed that when the staphylococcus attained an affinity for a certain structure of the body, a fresh subculture of the organism obtained from a focus of infection was apt to possess properties leading to its localization in that tissue.

The following remarks have reference to the production of arthritis by intravenous injection of a staphylococcus. The strain used was the one employed in the gastric ulcer series. It was obtained by blood culture from a case of septicaemia in man. At first, following intravenous injection of the organism into the general circulation of rabbits, the joints of the animals

showed no gross pathological change except a very occasional slight hyperaemia of the periarthicular tissues. However, cultures of the apparently negative joints very often yielded a pure growth of the staphylococcus. As negative joints in the early rabbits experimented upon appeared so regularly, examination for arthritis was gradually discontinued; but when rabbit No. 47, following upon an intravenous injection of a ten-day-old agar culture of the staphylococcus isolated from a stomach wall focus of rabbit No. 45, showed distinct lameness in the left hind leg, and at autopsy revealed an acute arthritis, routine examination for joint lesions was resumed.

The material used for injection was prepared by suspending an agar slant culture in about 10 c.c. of normal saline. The usual dose of such an emulsion was 1 c.c. for a rabbit and 3 c.c. for a dog.

In this series all but one animal (a dog) were rabbits. The following are a number of typical protocols of the animals injected after the staphylococcus had attained a sufficient virulence to cause acute arthritis.

Rabbit No. 47, wt. 900 grams, was injected intravenously with one cubic centimetre of saline emulsion made from a ten-day-old agar culture obtained from a stomach wall focus in rabbit No. 45. About 24 hours later, the animal showed lameness especially in the left hind leg, but otherwise seemed quite well. It was etherized and autopsied 36 hours after inoculation. The elbow joints show slight hyperaemia, joint fluid clear and apparently not increased in amount. Both knees are swollen and red. The redness in the right leg is limited to the joint, but in the left leg, it extends down to, and includes the ankle. Incision into the knee joints liberates a thick sanguinous fluid. The stomach, appendix and other organs are negative. Cultures from the joints on agar and in ascitic dextrose broth show a pure growth of the staphylococcus. Cultures of the heart's blood are negative.

Rabbit No. 48, wt. 1025 grams, was injected intravenously with 1 c.c. of the same emulsion used in rabbit No. 47. The next day the animal appeared lame, but otherwise seemed normal. On the second day after injection it was etherized and autopsied. The knees and elbow joints are red and swollen. The joint fluid is increased in amount, that of the elbow cloudy and of the knee purulent. Fresh smears of the fluid show leucocytes, red blood corpuscles and staphylococcus in pure culture. The appendix is very slightly injected and shows two small white areas, which from previous experience, are recognized as foci of the staphylococcus. There is one small abscess in the muscles of the abdominal wall. The kidneys appear slightly congested, otherwise normal. The heart and stomach are negative. Cultures on agar and ascites dextrose broth yield a pure growth of the staphylococcus.

Rabbit No. 56, wt. 975 grams, was injected intravenously with 1 c.c. of an emulsion of a 20-hour-old agar growth obtained by culturing knee joint of rabbit No. 47. About 72 hours later, the animal appeared very sick, and therefore, etherized

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† Experimental Production of Gastric Ulcer, BOSTON MEDICAL AND SURGICAL JOURNAL, May 11, 1916.

and autopsied. The knees are very much swollen and red. The joint fluid is increased in amount and semi-purulent. The other joints appear normal. The appendix is acutely inflamed. The distal half is turgid, diffusely hyperaemic and rigid. The proximal half shows little change from normal. The heart shows myocarditis. The kidneys, stomach, gall-bladder and skeletal muscles are negative. Cultures of the knee, heart's blood and appendix yield a pure staphylococcus growth.

Rabbit No. 57, half-grown, injected with 1 c.c. of emulsion of the strain used in No. 56. On the fourth day after inoculation, the animal appeared to be very sick. It died the same day and autopsy was made shortly after death. The knee joints are acutely inflamed. The joint fluid is increased in amount and cloudy. The elbows are injected but not appreciably swollen. The gall-bladder is distended and measures two by one-half inches. Its wall is oedematous and studded internally with small white nodules, that under the microscope, turn out to be colonies of staphylococci. The fluid contents of the gall-bladder is muco-sanguinous and tinged a pale olive green. A fine yellow sediment is found in the dependent portion of the bladder. Fresh smears of the fluid show staphylococci. Stomach, heart and appendix are negative. The kidneys are finely granular and yield a pure culture of staphylococci. Cultures of gall-bladder are also pure growths of staphylococci.

Rabbit No. 63, wt. 1025 grams, injected intravenously with 1 c.c. of an emulsion of a 24-hour old agar slant culture of knee of rabbit No. 57. Animal died about 72 hours later. Left elbow is hemorrhagic. Joint fluid is increased and turbid. Other joints are apparently negative. In the muscles of the legs and abdominal wall are numerous small abscesses. Heart shows myocarditis and endocarditis. Kidneys show a few very small abscesses. Cultures of all the joints, heart and kidneys are positive for staphylococci.

Dog, female, wt. 11 kilos., was injected into femoral vein with 3 c.c. of an emulsion of a 24-hour-old agar culture from knee of rabbit No. 56. The next day the animal seemed normal and ate about three pounds of meat. On the second day, after the injection, she began to look sick and moved about with little energy. On the third and fourth days, she would not eat and lay stretched out in her kennel. Her abdomen was tender, rigid and spastic on touch. The floor of the kennel was partly covered with recently coagulated blood. The animal was etherized and autopsied at the end of the fourth day, wt. 9 kilos. While being etherized, considerable dark unclotted blood was discharged by rectum. Knee joints show slight redness of periarticular tissue and cloudiness of joint fluid. Elbow joints negative. Stomach shows a few hemorrhagic erosions. The duodenum shows about two centimeters from the pyloric ring, a necrotic area measuring 6 x 7 m.m. The centre of it is a bleeding point and apparently the chief source of blood found in the lower bowel. There are numerous small hemorrhagic erosions throughout the duodenum. The ileum, jejunum and large bowel, except for the presence of blood in the latter, are negative. The appendix shows the mucosa to be thickly studded with punctate hemorrhagic elevations. The kidneys are congested, the gall-bladder is negative. Cultures of the duodenal ulcer,

duodenal and gastric erosions and appendix, show a mixed growth of the staphylococcus and colon bacilli. Culture of the heart's blood shows a growth of staphylococcus in pure form.

RESULTS.

The results shown by the protocols indicate that the staphylococcus is apt to localize in the joints and to produce typical lesions of arthritis, if the strain is of proper virulence. The organism recovered from the arthritic lesions has a decided tendency to again localize in joints.

In some cases the arthritis was the only lesion found at autopsy, but in other cases it was associated with one or more other lesions, namely, duodenal ulcer, appendicitis, cholecystitis, myocarditis, pericarditis, endocarditis, nephritis, colitis and myositis. These other lesions will form the basis of future reports.

According to these experiments, it seems to be true that while the organism used (a staphylococcus) may show a predilection for a particular region of the body, it will not always produce a gross lesion at the expected point of attack. In order to produce a gross lesion, it is necessary either for the staphylococcus to be of a certain grade of virulence, or for the tissue in which it has lodged to be suitably altered for the growth and action of the organism. This principle demonstrated itself repeatedly in the course of experimental production of gastric ulcer, and again in experimental production of acute arthritis.

REMARKS.

The results of localization obtained in connection with studies of staphylococci are singularly suggestive of Rosenow's† results with streptococci. A comparison of the total results in the two series will be made at a future time when the data are more complete. In the meantime, it seems worth the saying that if these facts apply in the cases of streptococci and staphylococci, it would seem to be possible that they may apply to still other organisms, for so far as we can determine, the essential factor governing localization, is growth in the tissue. After an organism has grown in a certain environment, it tends in later generation to select that environment, or at least, to thrive best in that environment.

CONCLUSIONS.

It has been pointed out in a previous communication that the staphylococcus may be caused very regularly to localize in the stomach after intravenous inoculation.

It appears that the same organism may be caused to localize in joints and produce typical arthritis.

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† E. C. Rosenow: Elective Localization of Streptococci, *The Jour. A. M. A.*, Nov. 13, 1915, p. 1688.