

the latter there was practically no typhoid fever. It was necessary to direct attention in another direction. It was found that a kitchen drain from Cottage B ran within about 15 feet of the well. On suspicion the well was accordingly closed, April 10, the day on which the location of the drain was found. Thereafter all water used in the hospital was boiled river water.

Exhumation showed the drain to be an open-joint earthen pipe laid many years ago, and honeycombed with leaks. The drain was crossed above by a sewer of poor construction which also drained a portion of Cottage B. Near the intersection was found an area of seepage from the sewer above to the kitchen drain beneath at a point where it ran nearest the well and toward it. No area of seepage was found from the reservoir mentioned above and the well. It is interesting to note that the employee F. J., the first suspicious case to appear at the hospital, was cook at Cottage B., where he resided. He had visited the town of Oswatome frequently during the time that typhoid fever was epidemic there. The patient D. F., who was the first case in the acute outbreak at the hospital, was an inmate of Cottage B. Examination of the well water showed the presence of *Bacillus coli*. No typhoid bacilli were found.

COMMENT

The most preferable way of dealing with institutional typhoid epidemics is to prevent their occurrence by means of a general immunization whenever typhoid is in the vicinity, or on the advent of the first suspicious resident case.

Routine inoculation of new patients and recently installed employees at stated intervals would conduce toward safety, and should be made the rule in any institution with a large resident population. This routine inoculation with bacterins can be made compulsory without serious objection on the part of patients or employees, and can be carried out speedily, effectively and with perfect safety.

It is impossible to determine absolutely whether the checking of the epidemic mentioned was entirely due to the use of typhoid vaccine or to the closure of the suspected well. From the recorded experience of others in the use of typical vaccines, and from the facts here reported, however, one is inclined to believe that the vaccine played at least a very important part in the control of the epidemic.

In any epidemic, all sources of food and water supply should be under suspicion and examined most carefully, no matter what their previous reputation may have been.

The Normal.—When we look broadly at biological phenomena, it is evident that they are distinguished by one universal characteristic. The structure, activity and life history of an organism tend unmistakably to maintain a normal. Accident may destroy an organism, or even a whole species, but within limits of external environment, which are the wider the more highly developed the organism is, the normal life history of each individual is fulfilled.—J. S. Haldane: "The New Physiology," *Science*, Nov. 3, 1916.

STREPTOCOCCUS INFECTION AS A CAUSE
OF SPONTANEOUS ABORTION*

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The belief that infection is a cause of recurrent spontaneous abortion and stillbirth is not original; in fact, the theory that it is the essential factor in many instances of "idiopathic" fetal death has a considerable number of adherents.

Study of the *Spirochaeta pallida* has already demonstrated one infectious organism which is directly responsible for death of the fetus in the later months.

That other varieties of bacteria should likewise possess the power of interrupting the course of pregnancy is to be anticipated. Conclusive evidence that such infections occur, demonstration of the characteristics peculiar to the invading organisms, and discovery of the foci from which reinfection develops in subsequent pregnancies, should do much to stamp out hitherto inexplicable cases of stillbirth. The object of the present report is to produce evidence which is helpful in the solution of this problem.

In the study of scurvy in guinea-pigs, streptococcus infection of the placenta was observed by Jackson and Moody. This reawakened interest in the old question of infection of the offspring through the placenta, and for the past year we have attempted to secure material for bacteriologic study from patients with spontaneous nonsyphilitic stillbirths. Such material is difficult to obtain; aside from some abortion cases in which criminal interference was evidently the source of infection, only the two cases herewith discussed have thus far been available.

REPORT OF EXPERIMENTS

CASE 1.—A patient, whose tonsils had previously been removed because of yearly recurrent tonsillitis, developed pyuria late in pregnancy and gave birth to an ill nourished child which died within twelve hours. Late in the following pregnancy, which occurred two years thereafter, pus again suddenly appeared in the urine. There was associated aching and a feeling of fulness in the region of the right kidney. A few days later, after spontaneous labor, a well formed stillborn child was delivered. The patient passed through an uneventful puerperium and was afebrile when I first saw her, two weeks subsequent to delivery.

Despite the mild nature of the vesical symptoms, catheterization was performed to determine the character and extent of the infection. Scattered pus cells and numerous cocci in pairs and chains (Fig. 1) were found in every field. In culture, hundreds of colonies of hemolytic streptococci developed.

This streptococcus produces hemolysis and grows freely in plate cultures. The microscope reveals a strongly gram-positive coccus, characteristically of rounded form, and of good size. Always in pairs, it often forms small clumps; on broth, and in condensation fluid, chains of considerable length occur. Litmus inulin is not acidified.

Injection of the patient with a small dose of autogenous vaccine (10 millions) was followed by a recurrence of lumbar

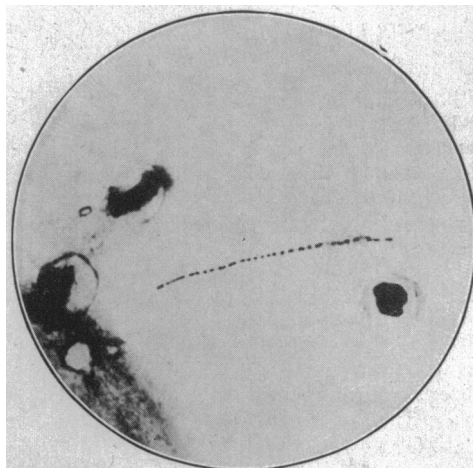


Fig. 1.—Streptococci in catheterized specimen of urine from patient with spontaneous stillbirth; Gram stain.

* From the Pathological Laboratory and Gynecological Service of St. Luke's Hospital.

aching and fulness, this time bilateral and most pronounced in the region of the left kidney.

A rabbit in the earliest palpable stage of pregnancy (from eight to twelve days) was intravenously injected with 2.5 c.c. of a washed ascites-broth culture. After an apparently normal course for six days, this animal was subjected to necropsy. Over 100 c.c. of clear fluid, such as Dick and I¹ found almost

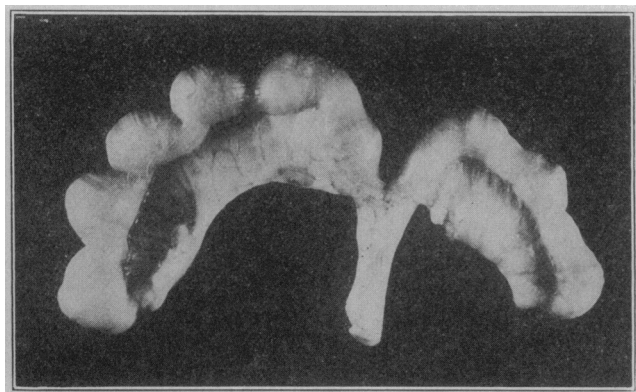


Fig. 2.—Bicornate uterus of a pregnant rabbit, containing fetuses undergoing absorption. Embryos less than one-half the size attained at time of intravenous injection, one week previously.

pathognomonic of early pregnancy in rabbits, were present in the abdominal cavity.

The uterine vessels were enormously distended. Two nodules were found in the right uterine horn, and at least two less distinct ones were present in the left horn. To Dr. Jackson, Dr. Moody and myself, the evidence was convincing that absorption of fetuses had occurred. The other viscera revealed no changes. Mediums inoculated with the ascites fluid remained sterile; from the heart's blood were obtained a few colonies of streptococci; from the kidney innumerable colonies of streptococci developed. Smears from the uterine cavity contained moderate numbers of the same organism. Histologic study of the uterus and other viscera will be subsequently reported by Dr. Jackson.

A rabbit two and a half weeks pregnant was intravenously injected with 2.5 c.c. of a washed ascites-broth culture of the streptococcus. The fetuses dwindled, in a period of seven days, from nodules the size of the rabbit's kidney to masses less than one-half as large (Fig. 2). Necropsy revealed that these numerous embryos were undergoing absorption (Fig. 3).

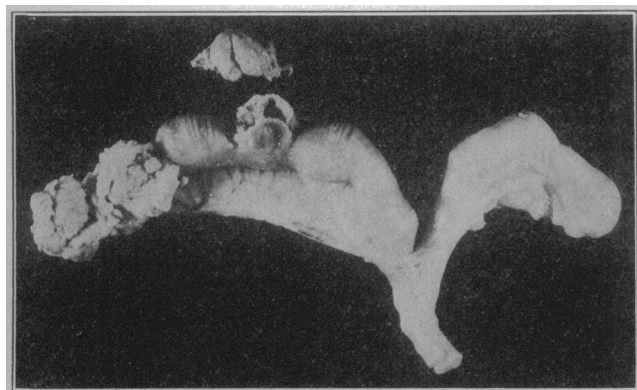


Fig. 3.—Uterus partially opened, with three necrotic embryos exposed to view.

Minute kidney abscesses, arthritis of the left knee joint, and an early lobar pneumonia were also present.

Fresh preparations and cultures from the uterine cavity and from the kidneys yielded the streptococcus in pure

growth. Mediums inoculated with free peritoneal fluid remained sterile.

CASE 2.—A patient of Dr. B. A. McBurney and Dr. De Lee, whose case was reported recently,² with history of a previous pregnancy with infection, gave birth to a stillborn fetus. At necropsy Moody found a streptococcus which he obtained in pure culture from the placenta and from the heart's blood. A subculture of this organism was used by me for further study.

Growth did not readily occur on plates, and hemolysis was not obtained on blood-agar slants. In other respects this organism is the counterpart of the streptococcus described in the preceding experiments.

A pregnant rabbit, near term, intravenously injected with 3 c.c. of a twenty-four hour washed ascites-broth culture of this streptococcus, gave birth to nine young on the following day. Of this litter four were dead and the five small remaining premature (?) young died within a few hours. The mother rabbit maintained the appearance of good health.

A month later, when two weeks pregnant, this rabbit was again intravenously injected with 3 c.c. of a twenty-four hour washed ascites-broth culture. After five days this apparently healthy rabbit was killed. In the uterus were found half a dozen retrogressing fetuses in varying stages of absorption. Smears from the uterus (Fig. 4) contained the streptococcus, which grew in pure culture in inoculated mediums.

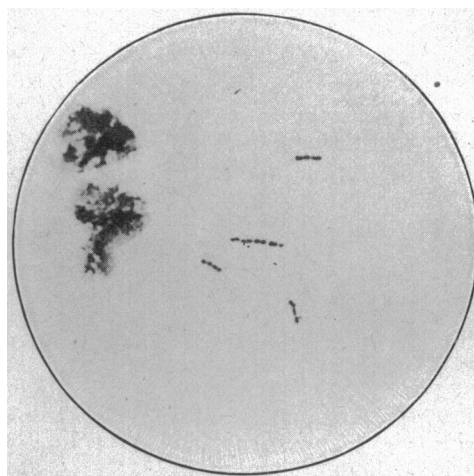


Fig. 4.—Streptococci in smears from the uterus of a rabbit containing fetuses undergoing absorption; Gram stain.

Another rabbit, slightly more than two weeks pregnant, was injected with 2 c.c. of a twenty-four hour washed ascites-broth culture. Five days later, palpation revealed evident retrogression of pregnancy. The rabbit seemed in good health, but was killed. At necropsy the uterus contained seven dead fetuses undergoing absorption. Smears from the lining of the uterus contained large numbers of the streptococcus. In cultures a pure streptococcus growth was obtained. These pathologic specimens were preserved for study.

COMMENT

From the urine of a patient who gave spontaneous birth to a stillborn child were obtained large numbers of streptococci. Two pregnant rabbits were intravenously inoculated with cultures of this organism. Death of the fetuses followed. One mother appeared to be in normal health, the other became seriously sick some days after the death of the fetuses. Pure cultures of the streptococcus were obtained from the kidneys and from the uterine contents of both animals.

From a spontaneous stillbirth were obtained pure cultures of a gram-positive streptococcus. A series of three pregnant rabbits was intravenously injected with washed cultures of this organism. In each instance

1. Dick, G. F., and Curtis, A. H.: Previously unpublished incidental findings in a study "Concerning the Function of the Corpus Luteum and Some Allied Problems," *Surg., Gynec. and Obst.*, November, 1912, p. 588.

2. De Lee, J. B.: A Bacteriologic Study of the Causes of Some Stillbirths, *THE JOURNAL A. M. A.*, July 29, 1916, p. 345.

there was premature labor or death of the embryos with absorption. Serious maternal illness was not evident. At necropsy, pure cultures of the streptococcus were recovered from the uterine cavity.

Whether organisms other than the streptococcus possess the power of interrupting the course of pregnancy does not materially influence these results. These facts remain: Streptococci can be isolated from women who give spontaneous birth to stillborn children; streptococci have been obtained in pure culture from the placenta and from the stillborn fetus; intravenous injection of pregnant rabbits with cultures of these streptococci is followed by fetal death; the streptococcus can be isolated in pure culture from the fetus and from the uterine cavity of the mother rabbit.

The streptococcus encountered in these cases appears to be peculiarly adapted to infection of the genito-urinary tract. Several closely related, probably identical strains, have been isolated from patients with uterine, tubal and kidney infections. Possessed of certain variability in cultural characteristics, these strains have much in common. We may have here to do with a type of streptococcus especially modified by, and with especial affinity for, growth in the genito-urinary tract; it is characterized by persistence of infection, low virulence, and richness of growth on artificial mediums.

SUMMARY

From the urine of a mother whose child was born dead, also from the placenta and heart's blood of a stillborn child, smears and cultures yielded large numbers of streptococci. Intravenous inoculation of pregnant rabbits was followed, in every instance, by abortion or absorption of the fetuses with recovery of the streptococcus in pure culture from the maternal uterus.

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THE TREATMENT OF CERTAIN DISEASES OF THE SKIN

BY THE INTRAVENOUS INJECTION OF A
FOREIGN PROTEIN*

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It is, no doubt, a common experience to observe beneficial effects in certain chronic conditions from intercurrent infections associated with high temperature. This we have observed in connection with certain diseases of the skin. One has seen the nodules of leprosy rapidly disappear after an intercurrent infection associated with high temperature: the bite of a cobra, as is well known, frequently causes a rapid resolution of the cutaneous lesions in this disease. One has seen psoriasis disappear during an intercurrent pneumonia, or typhoid; also the lesions of mycosis fungoides, after an intercurrent infection; we have artificially produced this in two cases by the injection of Coley's fluid (probably owing to the foreign protein). In one of them, the disintegration was so rapid that we fear it caused an earlier dissolution of the patient than would otherwise have occurred. A similar retrogression of lesions during hyperpyrexia has been observed in syphilis, and tuberculin has been

known to affect the efflorescence on the skin after a "test" injection.

Some years ago one of us suggested to a well known leprologist the injections of typhoid vaccine for the treatment of nodular leprosy, founded on the foregoing observed facts, with the thought that probably it was the hyperpyrexia which caused the resolution of the lesions, namely, that it was probable that the lepra bacilli did not thrive at a high temperature and that during a period of hyperpyrexia, though artificially



Fig. 1 (Case 1).—Condition of patient with psoriasis on admission.

produced, the organisms were killed, with subsequent involution of the lesions.

The artificial production of high temperature as an experimental method of treatment for various diseases of the skin has occurred to us several times in the course of years, but our thoughts on this subject were crystallized on reading an article by Jobling and Petersen¹ in which they review the subject of specific therapy in its relation to the production of certain changes in disease. They particularly refer to the "common clinical experience that some diseases, among them subacute joint diseases, neuralgia, diabetes, pernicious anemia, certain dermatoses, sarcoma, etc.," seem to receive distinct beneficial results following intercurrent febrile conditions, and they ask the question, Is it possible that these varied agents influence the course of disease by the production of high temperature?

From their investigations made at former times, they come to the conclusion that it seems probable that the remedial effects apparently produced under such conditions are due to "colloidal dispersion, in that the injections probably bring about a less dispersed state, affecting not only the serum proteins but also the serum lipoids." They go on to say:

Such an alteration is sufficient to account for the fluctuations in the ferment-antiferment balance and in the coagula-



Fig. 2. (Case 1).—Condition after injection; deep pigmentation only.

tion mechanism, as well as in the opsonic and complement powers of the serum, although it does not at present explain the increased antibody titer. . . . With this as a basis we can understand that so many and diverse substances can bring about a reaction almost identical clinically and therapeutically.

In other words, Jobling and Petersen believe that the beneficial effects produced in typhoid and in other

* Preliminary Report from the Barnard Free Skin and Cancer Hospital.

1. Jobling, J. W., and Petersen, William: The Nonspecific Factors in the Treatment of Disease, *THE JOURNAL A. M. A.*, June 3, 1916, p. 1753.