opened, it may delay degeneration in proportion to the density of the sheath. It would probably be advantageous to cut away as much as possible of the epineurium. A few experiments on the sciatic of any large animal would determine whether the interference with the blood supply is serious or not.

There are, no doubt, cases similar to those mentioned above in the nerve trunks supplying the arm. The only one dissected by Dr. Hashimoto and myself was the musculo-spiral (radial); in this the muscle division and the cutaneous division ran for a considerable distance isolated from one another, a fact which suggests that in cases of severance of the musculo-spiral the epineurium should be cut open and the two parts sutured separately.

REFERENCES.

- ¹ Kennedy, *Phil. Trans. Roy. Soc.*, B, 194, p. 127, 1901; B, 205, p. 27, 1914, and references there given. Osborne and Kilvington, *Brain*, 33, p. 289, 1911. ² Langley and Anderson, *Journ. of Physiol.*, 51, p. 372, 1904. Kilvington, *BRITISH MEDICAL JOURNAL*, September 16th, 1905. Osborne and Kilvington, *Journ. of Physiol.*, 37, p. 1, 1908; 38, pp. 268 and 276, 1909. ³ Langley, *Journ. of Physiol.*, 51, p. 388, 1917. ⁴ Langley and Hashimoto, *ibid.*, 51, p. 320, 1917. ⁵ Compton, *Journ. of Anat.*, 51, p. 103, 1917.

ANTENATAL SYPHILIS: SUGGESTED ACTION OF THE CHORIONIC FERMENTS.*

BY

AMAND J. ROUTH, M.D., F.R.C.P.,

CONSULTING OBSTETRIC PHYSICIAN TO CHARING CROSS HOSPITAL.

CONGENITAL SYPHILIS.

AFTER alluding to the discoveries of the *Spirochaeta pallida* by Schaudinn, the Wassermann reaction, and to the treatment by salvarsan, which can destroy the spirochaete without injuring the human tissues, Dr. Routh dwelt upon the serious nature of congenital syphilis as compared with primary infection, a positive reaction in a congenital syphilitic child hardly ever, according to Mr. Charles Gibbs, becoming negative under treatment. He alluded to cases of congenital syphilis transmitted to the third generation, as related by Dr. F. W. Mott, Mr. C. Gibbs, and Mr. J. E. R. McDonagh. He believed that not only is paternal infection of the ovum by the seminal fluid possible but that it is not infrequent, the mother becoming infected (1) either previously or at fertilization if she has a genital abrasion or erosion of the cervix, or (2) indirectly during the pregnancy via the embryo (conceptional syphilis), or (3) she is infected by spirochaetes in a granule stage, the mature organism being developed only after pregnancy.

More usually, he said, the embryo is infected by the already infected mother, either by the ovum being already infected, or by infection whilst embedded in the uterine mucosa, or by transplacental infection.

Sometimes there is a "mixed transmission" of infection from both parents. With very early abortions within two or three weeks of fertilization, following paternal infection of the ovum, it is possible that the woman may escape infection, owing to the absence of any true fetal circulation.

There is evidence (1) that infection can take place by the seminal fluid (F. W. Mott, etc.) even when the father has a negative Wassermann reaction, and (2) that the spirochaete has been found in the ovum in syphilitic women (Levaditi, Ball, and others). Dr. Mott has proved that syphilis is most contagious in its earliest stages, becoming less virulent each succeeding year owing to formation of maternal antibodies, the usual sequences of pregnancies being abortions, stillbirths, diseased children dying at birth or in early infancy, and children showing no signs of disease till puberty.

Dr. Routh believed that 25 per cent. of stillbirths and abortions in urban centres were probably due to syphilis, that if only 20 per cent. were caused by that disease in urban and rural centres in England and Wales, about 27,000 deaths would occur annually during the antenatal period and the first fourteen days after birth from that cause. The mortality of illegitimate children, both *in utero* and after birth, from syphilis was at least twice as heavy. The next most frequent causes of antenatal and natal deaths were toxæmia, *ante-partum* haemorrhage,

and dystocia. Macerated fetuses are, he said, now known to contain spirochaetes in over 80 per cent., though the mature organism is rarely found in abortions before the fourteenth week (Weber).

Many cases, both mothers and offspring, show no clinical evidence of syphilis till some weeks after the childbirth.

The Wassermann Reaction.

The Wassermann reaction, when first discovered, was expected to be positive when the individual was syphilitic and negative when uninfected or cured. Anomalies, however, have appeared and require explanation. Allusion was made to cases of syphilis during pregnancy with unexpected reactions, such as the negative reaction of some women when gravid with a syphilitic child, and for some time afterwards, and the negative reaction of some syphilitic children at birth, becoming positive a few weeks afterwards when the mature spirochaetes developed.

It is recognized, and has been especially stated by Mr. McDonagh, that pregnancy in some way or other often prevents the development of the mature spirochaete and that the disease is in these cases practically arrested in both mother and child during pregnancy. This, Dr. Routh believed, occurred more particularly in cases of paternal infection of the embryo. McDonagh even says that "repeated pregnancies have undoubtedly resulted in a spontaneous cure of the disease."

Some children may show no evidences of syphilis till they get tabs or general paralysis at puberty, whilst some mothers of these children may show no symptoms till after the menopause, or escape apparently altogether. The Wassermann reaction in these long latent periods has not been adequately observed.

All these cases require some other explanations than those usually given. The original words of Colles's law are true, though the numerous and varied explanations are often faulty.

Biology of Spirochaeta pallida.

Dr. Routh then reviewed the life-history of the spirochaete, giving extracts from Dr. Mott's article, in which O'Farrel, A. Balfour, and Noguchi are quoted, tending to show that under the action of salvarsan, etc., as well as spontaneously, the mature spirochaetal spiral becomes broken up transversely into granules, and that in a suitable environment these granules are capable of development into the mature organism after a short or long period of biological activity.

Noguchi had proved that after such granules have been transferred to a passive culture medium "spiral forms again sprout out." Dr. Mott has said:

The researches of Leishman on the spirochaete of tick fever suggest the possibility of an intracellular phase of the spiral organism, and its existence in the form of infective chromidian granules. Moreover, in support of this hypothesis I may mention that Neisser, in his experimental investigations on apes, has observed that the tissues of infected animals in which no spirochaetes were demonstrable, could nevertheless be used effectually for inoculation. The spirochaete may be one form of the syphilitic organism, but there may be other minute stages analogous to the spores of bacilli.

Infection by the granules can apparently occur during pregnancy, and if the granules are kept quiescent it is probable that the infected individual (mother or child) would give a negative Wassermann reaction after the birth so long as mature spirochaetes were absent.

If congenital syphilis is to be checked before the embryo is destroyed it must be dealt with locally at its source, and from the very first days after fertilization and infection. It seemed obvious that the embryonic tissues could not during the first few hours or days produce antibodies which could destroy spirochaetes.

Suggested Action of Chorionic Ferments upon Spirochaetes.

The great changes which occur in the maternal tissues, and especially in the ductless glands, Dr. Routh said, are only gradually produced, and are, therefore, not available in the early weeks to deal with spirochaetal infection. There are, however, locally present very powerful chorionic ferments produced by the syncytial cells of the fetal chorionic villi. These ferments are present in the early days of pregnancy at the point of interdigitation of the fetal and maternal portions of the placenta, and therefore

* Abstract of valedictory presidential address to the Harveian Society of London, January 10th, 1918.

are available as a powerful chemical filter for the protection of both mother and child. Their action is primarily trophoblastic to enable the delicate chorionic villi to penetrate the uterine mucosa at the placental site, and to open up maternal blood vessels, so that the ovum may have a resting place with nutritive blood spaces round it. As a result of the destructive action of the ferments upon the maternal tissues, syncytio-toxins are formed, but appear to be normally at once neutralized by so-called syncytio-lysins, and it is believed that if either of these bodies is in excess maternal and fetal toxæmia may result, often with fatal results. These ferments have been demonstrated chemically by Abderhalden to be present in the maternal blood till fifteen days after labour, and syncytio-lysin, or a maternal antibody, is demonstrable between the sixth and fourteenth week of pregnancy.

Dr. Routh suggested that these trophoblastic chorionic ferments are not only able to break up the infective spirochaetes into granules, but can, by their continued action, keep the granules quiescent and powerless to develop into the mature organism till after pregnancy, when the ferments soon cease to be present. The biological activity of the granules, unless restrained by other substances, would then be resumed, and mature spirochaetes would be developed.

He proposed explanations of the four following problems, founded on the spirillolytic action of the chorionic ferments:

1. Why may a pregnant woman who in due course either has a stillborn or a living syphilitic child have a negative Wassermann reaction during pregnancy and for some time afterwards?

2. Why are some syphilitic children negative at birth, and for some weeks afterwards?

3. Why are spirochaetes so rarely found in abortions, even though alternating between stillbirths, in the tissues of which they are swarming?

4. How do these suggestions of the spirillolytic action of the chorionic ferments help to explain the truth of the original words of "Colles's law"?

His conclusions were as follows:

CONCLUSIONS.

My suggestions seem to point to the following conclusions, some of which are scientific facts, whilst others are non-proven, but I think logical.

1. The "granules" are the result of the "spirillolysis," or breaking up of the *Spirochaeta pallida*.

2. The "granules" are infecting agents, being in fact spirochaetes in the granule stage. They are able to develop into the mature spirochaete in a suitable environment, or may become biologically inactive and remain latent for short or long periods.

3. Chorionic (syncytial) ferments are present at the point of interdigitation of the fetal and maternal portions of the placenta. Their action is primarily trophoblastic to enable the delicate chorionic villi to penetrate the uterine mucosa and to open up maternal blood vessels, so that the ovum may find for itself a resting place with nutritive blood spaces round it. As a result of the destructive action of the ferments upon the maternal tissues, so-called syncytio-toxins are formed, but appear to be at once neutralized by so-called syncytio-lysins. If not thus neutralized, maternal and fetal toxæmia may occur.

4. The chorionic ferments (or their derivatives) are suggested as being capable of exercising their destructive properties upon the *Spirochaeta pallida*, which may either be in the maternal intervillous, or fetal intravillous tissues, both of which are in intimate relations with the syncytial cells of the villi whence the ferments arise.

5. This destructive action of the chorionic ferments upon the spirochaete breaks it up into granules.

6. I further suggest that during pregnancy it is the continued action of the chorionic ferments upon the granules which may render them latent and biologically inactive, and perhaps in a few cases may destroy them.

7. After the pregnancy, when the chorionic ferments cease to be present in the tissues of the mother and child, the granules, wherever they may be, may develop into mature spirochaetes.

8. The success or failure of the chorionic ferments to protect the mother and child from spirochaetal infection would depend upon (a) the virulence of the infection,

which tends to diminish, owing to the presence of more maternal antibodies, with each successive pregnancy; and (b) upon the source of the infection. Infection is probably most difficult to arrest in a "mixed transmission," or in a true maternal infection, where attempts at infection of the embryo would be constantly proceeding throughout the pregnancy. It is probably least severe, and most easily countered by the ferments, when the primary infection is paternal, for it may then be a single infection only, and probably not capable of repetition if the primary infection be arrested.

9. The Wassermann reaction in mother and child appears to be negative if infection has been only by spirochaetes in the granule stage, so long as the granules remain biologically inactive and the mature organisms are absent.

THE COURSE OF INSTRUCTION IN VENEREAL DISEASES.

By DAVID WATSON, M.B., C.M.,

LECTURER ON VENEREAL DISEASES, UNIVERSITY OF GLASGOW.

IN view of the recommendations of the Royal Commission on Venereal Diseases, medical schools are faced with the problem of providing their students with special instruction on the diseases popularly included under the term "venereal disease."

The recommendations of the Commission as to teaching are summarized as follows in their Final Report (Sect. v):

(27) Whether by means of compulsory attendance at a course of instruction in venereal diseases or otherwise, it should be rendered certain that every medical student has adequate practical instruction in these diseases. Every medical student should attend a course of practical instruction in skin diseases.

(28) Questions relating to syphilis and gonorrhoea should be systematically set in medical and surgical examinations, so that the knowledge acquired in these diseases by candidates for examination may be tested.

As there is no class at present in the curriculum to which it would be possible to refer the teaching of this subject, the establishment of a new class will be found necessary, and the course will require to be compulsory, otherwise only a percentage of the students will attend. No expedient, such as including a question on the subject in one of the medical or surgical papers of the final examination, especially when such question is neither set nor checked by the teacher, will succeed in ensuring the attendance at a voluntary class of the majority of students. The General Medical Council may solve the question in one of the three following ways: (a) The establishment of a new compulsory class on the venereal diseases; (b) the inclusion of the teaching of the whole subject in a compulsory dermatology class; (c) the division of the subjects between a dermatology class and a new class of genito-urinary surgery, both compulsory. The last method would be the ideal one, but, unfortunately, in addition to imposing two new classes on the student, it is a plan which it would be possible to realize at present in few medical schools owing to the paucity of genito-urinary clinics. If medical education had been allowed to follow its natural process of evolution we would doubtless have found the teaching of syphilis allocated to the dermatologist and that of gonorrhoea to the genito-urinary surgeon. But circumstances have combined to force the pace in another direction, and with attention focussed on venereal disease while genito-urinary surgery lags behind, it must be recognized that the attempt to carry out this plan would involve intolerable delay.

Of the remaining alternatives there is much to be said in favour of the venereal diseases being included in an enlarged dermatology course. By this procedure the interest of the patient, the student, and the teacher would seem to be best served. The students' curriculum is extended by the minimum, while both recommendations in Clause 27 are complied with, the patient escapes the stigma of attendance at a purely venereal clinic, and the teacher is released from an undesirable curtailment of his sphere of work. On the other hand, it will doubtless appear to the governing bodies of many medical schools that the simplest and most direct way of dealing with the question