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RECENT RESEARCH IN CONNECTION WITH VENEREAL DISEASE

By Dr. T. E. OSMOND

DISCUSSION

Dr. T. ANWYL DAVIES expressed his thanks to Dr. Osmond for his paper, and said he would carefully study the references given. He asked whether the reader could throw some light on the peculiar serological reactions, for example, where the Wassermann was always positive while the Kahn remained persistently negative, and vice versa. Frequently cases of clinical syphilis were seen in which, persistently, the Wassermann was negative and the Kahn positive.

He asked whether members had had experience following the use of devegan of rashes and deep ulceration which started like bullous pemphigus. He had seen 4 such cases.

He had been interested in the finding in new-born children of spirochætes in the umbilical vein, although the blood test was negative. The umbilical vein being fairly fresh tissue, one would expect the Wassermann to be positive. It seemed to favour the belief that a positive Wassermann did not necessarily mean that living spirochætes were present.

The increased power of arsenic, bismuth and mercury when added to a positive serum in vitro so that the reaction became negative suggested that mercury was as effective—if not more so—than bismuth. He would like Dr. Osmond’s opinion.

His experience with salvarsan was much the same as that quoted.

COLONEL L. W. HARRISON said he could well understand the difficulty Dr. Osmond had experienced in preparing such a paper at short notice, and he congratulated him on the labour and energy he had shown in achieving the result.

As to the advantage of carrying out more than one serum test for syphilis, on the principle of founding
the diagnosis on as broad a base as possible, T. Grüneberg recently drew particular attention to a test which had been devised by Gaehtgens, in which the antigen was a watery extract of alleged *Spirochaeta pallida* in saline with 0.3 per cent. phenol. It was claimed that this was definitely a test of anti-spirochætal substance, whereas the Wassermann and the flocculation tests depended on an anti-lipoid in the serum. Grüneberg said that he could produce an antibody to cultural *S. pallida* by inoculating normal human beings with this watery extract of it in the phenol solution. He had also stated that syphilitic patients who had given a positive pallida reaction as a result of their natural infection showed a negative phase after commencing to be inoculated with the pallida antigen, so that, temporarily, the reaction against the pallida was less. If that was so, it suggested that one might supplement the Wassermann test, not with one of the ordinary flocculation tests, but with one in which a spirochætal antigen was used. If that was successful, one wondered how it tallied with the opinion of Kolmer and his colleagues that the so-called cultures of *S. pallida* were not *S. pallida* at all.

Speaking about new work on lymphogranuloma inguinale recalled to him a question raised by the writer of a recent paper as to whether that disease was transmissible to the offspring. The author had suggested that people might look out for cases which would eventually assist a decision on the point. He had reported 2 cases, one in a woman who had obviously suffered from lymphogranuloma inguinale for three years and gave it to her infant, who, two weeks after birth, gave a positive Frei reaction. The speaker wondered whether that was a transient reaction. The other was the case of the daughter of a woman who in 1906 had come under observation with symptoms clearly due to L.i., though in 1906 there was no skin test for it. A daughter, now aged 14, came up first because of rectal stricture. That was excised, and later—after some years—she came again, and the Frei test was strongly positive. It was obvious that the daughter of this patient suffering from lymphogranuloma inguinale had herself got it from her mother, but how it had been transmitted was not suggested by the author of the paper.
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Dr. Orpwood Price also congratulated Dr. Osmond on his paper. Among all the research workers mentioned in the paper he regretted that only one was a Britisher; he did not know whether that meant more research work on the subject was done abroad than in these Islands. If so he could see only one reason for that, namely, that in this country research workers were not supported as they should be. On the other hand, it might be urged that foreigners were more ready to rush into print.

With regard to serum tests for syphilis, in the White-chapel Clinic they always did a Wassermann and a Kahn as a routine, and in cases of doubt a Sigma. In difficult cases they did this third test, on the principle that the more evidence one could obtain the better.

As to culturing the gonococcus in an atmosphere of CO₂, he was surprised the lecturer did not mention the work of McLeod and his co-workers, which had been recently published in the Journal of Pathology and Bacteriology. As a practical point, the speaker did not see how the clinician could guarantee an atmosphere of 8 per cent. to 10 per cent. CO₂. When inoculating it was better to burn the end of a cotton-wool plug, and, when it was smouldering, put it back in the tube. One would see a column of smoke, and this appeared to assist the growth of gonococci; it could be done without apparatus and without working out any degree of concentration of CO₂.

No doubt many cases of Trichomonas vaginalis were being missed. Usually it was easy to diagnose the condition in patients if the discharge was examined under dark-ground illumination or a ¼ lens. If this could not be done at once, a plan which worked fairly well was to put some vaginal discharge into a test-tube with 5 c.c. of normal sodium chloride, leave it at room temperature, and then twenty-four to thirty-six hours afterwards it could be examined under the microscope, and one would find typical movements of the membrane, and there would be no difficulty in identifying the parasite.

Colonel E. T. Burke wished to add his thanks to those expressed by others for Dr. Osmond's paper. A tremendous amount of clinical research had been going on in this country and in others. Why, therefore, did one hear only about laboratory research? The clinician was only too keen to profit by the results of research.
carried on in the laboratory; but he did not think the
laboratory worker was always keen and anxious to be
of service to the clinician in the many problems which
puzzled him. A closer liaison between the two spheres
was indicated.

Dr. Osmond had mentioned mapharsen. The speaker
had tested it in his former clinic, and the conclusion was
that it was definitely inferior to arsphenamine, but was
about equal to one of the lip-soluble bismuth compounds.

With regard to Dr. Osmond’s remark about syphilis
occurring during the Ming dynasty, and that chancres
had been known in China from time immemorial, he
was in entire disagreement; if those cases were syphilis,
then it was a peculiar syphilis which did not cause
congenital syphilis, nervous or bony lesions or aneurysm.
It was only after the beginning of the fifteenth century
that these conditions were recorded as occurring in China,
thereby indicating that syphilis did not exist in that
country prior to that date.

Dr. Kathleen Brown, after thanking Dr. Osmond
for his paper, said she was interested to hear Dr. Anwyl
Davies mention infection with the Trichomonas vaginalis.
She had found the infection present in some patients
who were attending either for investigation of a vaginal
discharge or for treatment of gonorrhoea. The typical
discharge responded well to local treatment, but relapses
were common within a few days in some cases or in three
or four weeks after treatment had ceased.

She wondered whether the trichomonas were always
present and only gave rise to symptoms at intervals.
She had found that devegan cleared up the condition
better than did anything else.

Mr. Ambrose King said he would like to be given a
clear idea of the criteria by which a false positive sero-
logical reaction might be judged. It was agreed that the
absence of a history or of symptoms of syphilis, or the
absence of active signs, did not mean that the disease
was not present. Cases were common in which serum
reactions were positive but no signs or symptoms of
syphilis could be found. Laboratories had been known to
differ in their results when testing the same sera. How
was the clinician to interpret such results, and when
might they be disregarded?

With regard to vaginal infection with the Trichomonas
vaginalis, Dr. Brown had mentioned the difficulty of permanently eliminating it with devegan. He had also experienced that difficulty and had known recurrences, particularly after the menstrual periods and during pregnancy. He thought that this might be due in some cases to the presence of the gonococcus in addition to the trichomonas parasite. In recent years most of the literature on the subject of trichomonas infection had either omitted all mention of gonococcal infection, or had stated that the concurrence of the two infections did not take place, or was rare. That, however, had not been the experience of himself and his colleagues; indeed they had been able to isolate the gonococcus in over 40 per cent. of a series of 70 cases of Trichomonas vaginalis. The protozoon tended to mask the presence of the gonococcus and to make the isolation more difficult.

Dr. Osmond had truly remarked that there was little to report about research in connection with gonococcal infection. It was only too evident that most of the attention devoted to venereal disease was concentrated on syphilis and diseases other than gonorrhoea. The latter was a most neglected disease, and the present methods of treatment were positively mediaeval. He wondered how much was being done to remedy this state of affairs and whether research in this important subject was receiving the support that it deserved. The lack of adequate research was shown in the Report on the Gonococcus and Gonococcal Infections recently published by the American Medical Research Council in conjunction with the American Social Hygiene Council. It was there estimated that only twelve centres in the whole of the United States were carrying on research in this subject. Another estimate said that over a million fresh cases of gonorrhoea occurred in the United States every year. That, surely, was an appalling state of affairs and one for which the present ineffective modes of treatment must in great measure be responsible.

MR. V. E. LLOYD also wished to compliment Dr. Osmond for his interesting and very stimulating paper. He had been particularly interested in the reference to Ingraham's work upon the methods of examination for Spirochata pallida in the umbilical vessels of the new-born child.

For some time he, Mr. Lloyd, had been actively
interested in this subject, and some months ago had inaugurated a service by which a small portion of the umbilical cord of every child born in the Maternity District of Guy's Hospital was sent to the V.D. Clinic on the same day for examination. The piece of umbilical cord was sent up in an envelope and no special methods of preservation were employed.

On receipt the small piece of umbilical cord was cleared of blood and pegged out on a board. The umbilical vessels were slit up and by teasing through a small drop of saline an emulsion of the endothelium of the vessels was prepared. This emulsion was then examined for Spirocheta pallida by the method of dark-ground illumination.

So far about thirty cases had been examined in this manner, but no cases of syphilis had yet been dealt with. It is hoped that this method, which is very simple, will prove to be the most rapid method of ascertaining whether the new-born child has syphilis or not.

Although he had not utilised safranin in the detection of Trichomonas vaginalis, he had had excellent results with eosin, in a concentration of 1 in 500. This solution lightly stained the leucocytes and epithelial cells, but did not colour the trichomonads and did not interfere with their movements.

GROUP CAPTAIN H. E. WHITTINGHAM said that he was surprised that no mention had been made of the Meinicke reaction. This test gave as accurate a diagnosis of syphilis as the Wassermann, Kahn or Sigma reactions, especially if both the macro- and microscopic methods were adopted as a routine. Strict adherence to technique was necessary, as was the case with the other tests mentioned. The test was so simple, requiring the minimum of apparatus, and there was no difficulty in reading results, which were available in one hour. It was certainly an ideal preliminary test to use in conjunction with the Wassermann reaction, and was of utility especially for work in the tropics, where antigen and complement tend to deteriorate quickly.

With regard to malaria per se causing a positive Wassermann reaction, he was far from satisfied that this was the case. In the Royal Air Force, since its inception in 1919, a Wassermann test was done on all those invalided from overseas, and of the many hundreds of malaria cases
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examined since then and previously he had only had one with a positive Wassermann reaction where syphilis was not present as well. When one considered life in the tropics and sub-tropics, one should not be surprised to find a certain number of unrecognised cases of syphilis amongst those suffering from malaria.

He mentioned that trichomonas and other flagellates could be readily seen with the aid of the ½ objective if stained either with 1 per cent. eosin solution, Gram's iodine or a mixture of the two, as recommended by Donaldson many years ago. With Donaldson's solution the flagellates and other protozoa stand out as greenish bodies against a red background.

With regard to the culture of the gonococcus, it was common experience to find that this organism could be readily grown in one laboratory, while in another there was failure even when using similar types of media. The reason for failure was usually errors of technique, especially in the preparation of media which was too often left in the hands of assistants. Failures could be overcome by obtaining the correct pH reaction of the media, together with a reduction of the oxygen content of the tube by heating its upper end and singeing the wool plug.

Mr. Claude Mills said that the remark of the last speaker, concerning the large influence that malaria was credited with having upon the Wassermann reaction, reminded him of an investigation which he had carried out, in conjunction with Professor John Thomson of the London Tropical School, several years ago upon this assumption.

We investigated a large number of cases of malaria, comprising different types of infection, some under treatment, some not, and in none of these was the Wassermann reaction found to be positive as a result of malaria per se. In those instances where the reaction was positive it was proved definitely to be due to syphilis—not to malaria.

Dr. Facey asked whether Dr. Osmond had observed any special characteristics in the clinical appearance of cases of male trichomonas infection. In the female the discharge in that disease was often frothy, and other signs were present which caused one to suspect that infection. He also would like to know whether pessaries for vulvo-vaginitis were on the market.
He did not know whether work had been done on the allergic state in venereal disease generally; it must be a very important factor in both syphilis and gonorrhoea. He believed it was recognised that salvarsan dermatitis of allergic causation occurred, and he thought that some of the complications of gonorrhoea closely suggested allergic reactions, particularly some forms of gonorrhoeal arthritis. If so, what were the factors which produced an allergic state? Presumably the hereditary factor was one, and a septic factor was another. Usually patients exhibiting these allergic symptoms had foul teeth, or some other septic focus.

The President said that certain points in the paper had interested her particularly. She was intrigued by the scraping of umbilical veins of new-born children in the search for spirochaetes, and when her maternity ward was reopened that procedure should be carried out in every case in which the mother had been treated for syphilis. She and her colleagues had noticed that the new-born baby of the mother who had been fairly well treated for syphilis nearly always gave a negative Wassermann, and yet in a few months might develop a positive Wassermann, or die of some inter-current condition, found to be syphilitic unless it had been previously treated. Therefore she paid little attention to a negative Wassermann in a child in early weeks when the mother had been actively syphilitic.

She was also interested in X-rays on the long bones being used as a means of early diagnosis of syphilis. Dr. Chodak Gregory, who was in charge of the Children's Department at the Hospital, was very keen on that method, and Dr. Rorke and she had had many arguments over films as to whether they indicated syphilis or not.

As to CO₂ helping in the culture of gonococci, her query was as to how to get the CO₂ in. She flamed the inner end of a cotton-wool swab, and that must make some CO₂.

In the treatment of trichomonas infection most used devegan, but that, of itself, was not enough; unless there had been a previous cleansing of the canal the symptoms tended to recur. She was much interested in what Mr. King said about trichomonas infection and gonorrhoea. She read a paper by a woman in America who had been working on the subject, and in that it
was stated that in 50 per cent. of cases trichomonous infection was present with the gonococcus and a large percentage of secondary organisms.

What Dr. Osmond said about the general treatment of gonorrhoea had aroused her into saying what she had long wished to, namely, that the treatment of that disease was appalling. Research on this had simply got to be done. The chief barrier to real research on it seemed to be the lack of money; she wondered whether anything could be done to make a real start to put the treatment of gonorrhoea on a sound basis.

Dr. Osmond, in reply, said he thought all the speakers had misunderstood him, as he had scarcely given his own views at all. He agreed with Dr. Anwyl Davies as to the cases in which the results of the flocculation test and the Wassermann test seemed to contradict each other. He had always said he would "back" Colonel Harrison's Wassermann test against any other. One obtained more non-specific results with the flocculation than with the complement fixation tests if the latter were carefully controlled.

With regard to the effect of mercury and bismuth on serum, converting it into negative in vitro, that was not the same as in vivo. It did not follow that mercury was more active than bismuth.

Colonel Harrison's remarks about pallida antigen were very interesting. As to cultures of Spirocheta pallida, probably none of them had been pure cultures, therefore one did not know what the pallida antigen contained. But it was interesting to adopt another line of serological diagnosis. One had the Wassermann and the flocculation tests, which were tests for lipoids, and this was the true antigen to the antibody, so something could be said for it if a sufficiently sensitive antigen could be prepared.

Congenital lymphogranuloma inguinale was new to him, but it was an attractive idea; it might be a generalised disease early, as syphilis was.

He agreed that most of the research workers were foreigners; he apologised for not having mentioned McLeod's work, but Neumann gave that gentleman full credit for the discovery about diminished oxygen tension and the atmosphere of CO₂. His method was well worth trying.

Colonel Burke and he were in accord in regard to
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research. Research work did not belong only to the pathologist, and that was why he quoted some pieces of research which were purely clinical. As to syphilis in China in the Ming Dynasty, he did not say they had real chancres in pre-historic times; it was what Gear said. Also his remark about searching for spirochaetes in the umbilical vein was a quotation. Against X-rays as a means of diagnosis was the expense; there was also the question of interpreting the skiagrams.

Meinicke's reaction he admired very much. At St. Thomas's one got many specimens to do in a week, so one had to limit the number of tests, i.e., on each case. Kahn seemed to be the most practicable; it was simplest to put up and quickest to perform, though not the easiest to read.

He did not think any considerable proportion of malaria cases gave a false positive reaction; no test should give 8 per cent. of false positives in malaria. He did a fair number in India, and he had had some sent him since; he did not get a positive in any case which was not afterwards proved to be syphilis.

Gonococcus media were of two kinds—good and bad; mostly they were bad. Given the right media, gonococci would grow well. He had a laboratory man who was a first-class medium maker. He did not know why most text-books said the gonococcus was difficult to grow. pH 7.5 he thought was best, though with 7.3 one could go forty-eight hours without sub-culturing.

Dr. Facey should discuss with Dr. Clements as to gelatine pessaries.

Mr. King had raised the bogey about false positives; he, the speaker, thought there might be about one positive in a thousand which had not got syphilis.

The President had referred to the possible life-cycle of the Spirocheta pallida, and instanced the statements of McDonagh. It might account for a number of things, and one was Wassermann-fastness. If the Spirocheta pallida could go into a form of spore it might be that this spore was not influenced by the remedies used, and that might account for some cases which did not react to treatment. Levaditi and others tried treating tissue containing Spirocheta pallida, and tissues in which that organism could not be demonstrated, by using Gamma rays of radium, and the mercury vapour lamp and gly-
cerine, to see if they could demonstrate the difference between the two, but nothing came of it.

He agreed it was scandalous that lack of funds was such a barrier to research in this country. People would contribute for research into tuberculosis and cancer, but not venereal diseases. Yet research into gonorrhoea was most important of all. A good deal would probably be heard about that in the paper next month; he referred to the work going on in America with the hypertherm; temperature was kept high for some time, and remarkable results were claimed from it.