TRANSIENT NON-SPECIFIC WASSERMANN AND KAHN REACTIONS IN A CASE OF INFECTIVE HEPATITIS

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This case and its laboratory findings are reported to show that, so far as careful investigation can indicate, falsely positive Wassermann and Kahn reactions may occur during the course of infective hepatitis and disappear during recovery. The case was one of a large series met with while working on a routine scheme for investigating jaundice and liver enlargement without jaundice which included serological tests. The other cases in the series and their laboratory investigations will be dealt with in a further communication.

Case Record

The patient, an unmarried female aged 21, suffered from nausea, heartburn, and vomiting for six days before admission, when she began to be jaundiced. Her urine was dark and she was constipated. She had not felt well for the previous four weeks and did not go to work for three weeks before admission. Four months

reaction (fixing 3 M.H.D. of complement when diluted 1 in 2) and a suspicious Kahn reaction after a fortnight, and negative reactions by both tests after 27 and 70 days; also, the examination of the cerebrospinal fluid yielded negative results. From these as well as from the lack of historical or clinical grounds one must conclude that the reactions were transient biological falsely positive ones. These findings stress also the necessity for carrying out quantitative serological tests, and repeating them should they be found positive, especially when there is a negative case report—in spite also of the fact that in this case two reactions were positive, which is generally accepted to mean the presence of syphilis.

Biological falsely positive reactions may occur with all tests in the absence of syphilis (because of the presence in the serum of a reagin (Kolmer) similar to that present in syphilis), in yaws 100%; leprosy 40 to 80%; malaria 12 to 20% or higher, depending on the stage; infectious mononucleosis 20%. Positive reactions may also be obtained in relapsing fever, rat-bite fever 50%, possibly in Weil's disease and typhus. Furthermore, biological falsely positive reactions may occur in various acute infections, including pneumonia, though their incidence is probably less than 1 in 4,000 (Kolmer and Tuft, 1941). It is a widely held opinion that one can get non-specific reactions in cases of jaundice, but the literature does not support this.

Table showing Results of Laboratory Investigations

No. of Days after Onset of Jaundice	R.B.C. Hb Colour Index	C.V. M.C.V. M.C.H.C.	W.B.C. Lymphs, Monos., Eos., Basos	Platelets	B.S.R., Wintrobe, in mm./hour	Blood Urea in mg./100 ml.	Van den Bergh D=Direct I=Indirect mg./100 ml.	Alkaline Serum Phosphatase in King and Armstrong Units	Takata-Ara Test	Formol-gel Test	Serum Proteins, Total, Albumin, Globulin, Alb./Glob.	W.R.	Kahn	Urine	Miscellaneous Investigations
1	5,100,000 95% 0.94		7,500 58% 38% 2% 2%	Normal	2	32	D = + I = 5	17	++++	+ after 3 hours	6.5% 3.1% 3.4% 0.91/1	+++ in 1/40 dilution of serum	++	Protein: very faint trace Urobilin, — Urobilinogen, — Bilirubin, + Bile salts, +	Blood sugar 80 mg./100 ml.
14	4,700,000 90% 0.95	41% 87 c μ 30%			29		D = weak + I = 0.75					+ in 1/2 dilution of serum	Incomplete negative		C.S.F.: Protein, 40 mg./100 ml. NaCl, 680 mg./100 ml. W.R., — Lange, — Pandy, —
27						20	D = weak + I = 0.4	13	+++	—	8.5% 5.9% 2.6% 2.3/1	—	—		
34	4,640,000 88% 0.96														
70	4,500,000 90% 1.0	40% 89 c μ 31%	11,200 57% 38% 3% 2%	Normal	23	28	I = 0.2	8.5	+++	—	7.7% 5.6% 2.1% 2.7/1	—	—		

previously she was working in a factory where telephone cables were coated by a spray process, but she emphasized that she herself had not come into contact with the chemicals used. Her past history revealed only a Bell's palsy two years ago. There were no history of venereal disease, no family history or recurrence of jaundice, and no probability of Weil's disease. The patient had not been abroad. Apart from the above-named symptoms on admission, no abnormalities were found at the examination. Menstruation was normal, and gynaecological examination revealed no abnormalities or any signs of venereal disease. For a few days she was rather ill and dehydrated, and was still vomiting, the urine being dark and the motions clay-coloured. Then she made an uneventful recovery, the jaundice fading in three weeks. The temperature, apart from a slight pyrexia of 99.8° on admission, was normal throughout her stay. In addition to the usual routine treatment for infective jaundice the patient was given haematinics and ascorbic acid. She was discharged on the 36th day after admission and was seen again, symptom-free, on the 70th day.

Discussion

The Table shows that there was a strongly positive Wassermann reaction (fixing 3 M.H.D. of complement in dilutions of serum up to 1 in 40) and a positive Kahn reaction one day after the beginning of jaundice, a weakly positive Wassermann

A survey of tests conducted by Cummings *et al.* gives the following figures: neoplasms, 0 to 1.7%; fever (natural or induced), 0 to 2.3%; jaundice, none; pregnancy 0 to 1.9%; menstruation, none; active tuberculosis, 2%. Another survey (venereal disease information, as quoted from Gradwohl, 1943) does not mention jaundice at all. Harrison (1931) and Kampmeier (1944) also refer to the widespread opinion of the occurrence of falsely positive reactions in many conditions, among them jaundice, based on the older literature; but they could not confirm these findings, and relate them to errors in technique (see also Kolmer and Tuft, 1941). In this connexion the occurrence of falsely positive reactions due to smallpox vaccination seems worth mentioning (Lynch *et al.*, 1941).

Of 86 cases of the series, in which in addition to liver function tests serological tests were also performed, the reported case is the only one which gave transient positive reactions. The series included acute hepatitis, 35 cases (infective jaundice, 19; post-arsphenamine jaundice, 11—one died of acute necrosis of the liver; post-plasma-transfusion jaundice, 3; post-malarial jaundice, 1; Weil's disease, 1); subacute hepatitis, 3; obstructive jaundice, 20 (carcinomata with and without secondaries in the

liver, 17; gall-stones, 3); cirrhosis of the liver, 3; congestive heart failure, 7; amyloid disease, 3; amoebic disease, 2; carcinoma of the prostate, with secondaries of bone 1, and liver and bone 1; and miscellaneous 11.

The serum protein estimations show a disturbance of the albumin/globulin ratio one day after the jaundice began, which is also apparent from the very strongly positive Takata-Ara reaction. The high globulin value is also confirmed by the positive formol-gel test. There occurred also a flocculent turbidity after addition of water to the serum at the beginning of the protein estimation, which reminds one of the Klausner test. The later-performed investigations show a return to normality. This type of result is not uncommon in cases of hepatitis and other conditions, but one does not find positive Wassermann and Kahn reactions; thus one cannot merely on this basis explain the occurrence of the transient positive serological reactions. Do the findings in this case point to a special combination or pattern of lipoid-globulin which produced the biological falsely positive Wassermann and Kahn reactions?

Summary

A case of infective hepatitis with transient biological falsely positive Wassermann and Kahn reactions is reported. Reference is made to the widespread belief that this occurs fairly often in hepatitis, but the literature does not support this opinion. Other laboratory findings discussed are those which may have some connexion with a non-specific serological reaction.

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SUCCESSFUL SURGICAL TREATMENT OF ENTERIC GROUP CARRIER

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Over a period of years, up to January, 1944, sporadic cases of paratyphoid fever occurred in the Caldbeck district of Cumberland. The majority of these were among women in late pregnancy or recently confined. Between May, 1940, and December, 1943, four such cases of paratyphoid fever occurred in this area. There were one or two others among patients not belonging to this group. Certain of the cases terminated fatally.

The presence of a carrier in the district was suspected, but it was not until December, 1943, when the fourth of the cases among pregnant women occurred, that a pointer appeared indicating the possible location of a carrier. This fourth case, which terminated fatally, occurred in an adjoining village, which, while being in the area of the Caldbeck Nursing Association and within the practice of the Caldbeck doctor, was nevertheless quite distinct from Caldbeck village, and generally could be regarded as an extraneous area with little or no direct connexion with the area in which previous cases had occurred. The new common factor arising out of this fourth case was the attendance of the same doctor and the same district nurse-midwife.

Carrier's Case Record

A conference was held between the public health medical officers concerned and the practitioner. As a result investigations were carried out at the Cumberland Infirmary pathological laboratory in respect of the doctor and the district nurse, and cultures of *Bact. paratyphosum* B from the faeces and urine were obtained in the case of the nurse. The Vi and O agglutinins were negative, which is of interest in view of the belief that a chronic carrier usually has both to a high titre, and this test is frequently being used as a sieve to separate out chronic carriers, on the assumption that it is useless to examine Vi-negative cases. Investigations carried out during the

succeeding months proved the nurse to be a true chronic carrier. She has maintained throughout that she was not the source of the other cases, but was herself a victim of the disease acquired in the area. The question, however, is academic. She was suspended from the practice of midwifery, and ceased work as district nurse in the area. She entered the Carlisle Infectious Diseases Hospital for further investigation and treatment in January, 1944, and remained there as a patient until October, 1944. During the eighteen months which have elapsed since this nurse left Caldbeck no further cases of paratyphoid fever have occurred.

Dr. Felix, of the Ministry of Health laboratory, typed the *Bact. paratyphosum* B cultures by bacteriophage methods, and classified them as 3a. The cultures from the fatal case and two others which had subsequently occurred in the Caldbeck area—one being the parent of the fatal case—were, as would be expected, also 3a, proving that these were all infected by the same organism. By a fortunate chance the Cumberland Infirmary laboratory still had three other cultures of *Bact. paratyphosum* B, which had been obtained from cases that had occurred in Caldbeck, and had been dealt with in that laboratory, since 1940. These were also found to be type 3a. Of these three, one had been isolated from a puerperal case in March, 1943, which had been attended by the same nurse. The other two cases arose in 1940, both of them being in children. The cultures from cases of paratyphoid B investigated prior to 1940 were dead and could not be resuscitated. This was unfortunate, as it would have been interesting to find out if type 3a had existed in the area before the nurse took up duty in 1938.

From January, 1944, until October, 1944, the stools were examined at weekly intervals, and these always gave a profuse growth on desoxycholate media. During this period the nurse had two full courses of sulphaguanidine, which, as anticipated, had no effect on the condition. After admission to the Infectious Diseases Hospital she was x-rayed in February, 1944; her gall-bladder did not fill, indicating that some pathological condition was present. She was strongly urged to have a cholecystectomy done, but was unwilling to agree to operative treatment except as a last resort. In June, 1944, the first attempt was made to obtain a sample of her bile. A duodenal tube was passed, but owing to pylorospasm it would not enter the duodenum. While the tube was in the stomach she was x-rayed, and in spite of atropine and gastric massage it did not pass into the duodenum. Culture of the gastric juice was sterile. After giving magnesium sulphate a small quantity of bile-stained fluid was obtained. This, however, was strongly acid, and was sterile.

Dr. Felix, at this point, suggested a vaccine rich in Vi and O antigens. This was given intravenously in graduated doses in July, 1944. The patient had a considerable reaction, with a striking rise in the titre of her H and O agglutinins in the blood to 1 in 1,000 and 1 in 5,000 respectively. The Vi titre was 1 in 20. Her stools, however, remained positive. In August a duodenal tube was successfully passed. The gastric contents were negative, but the duodenal juices, after the administration of magnesium sulphate, yielded a growth of *Bact. paratyphosum* B. In September a second course of injections of intravenous vaccines was given, after which the stools were still positive, and the titre of the agglutinins in the blood remained the same. The mental condition of the patient had by this time altered. She was depressed and wept frequently, and had the impression that nothing effective in the way of treatment was being carried out. She still refused to have her gall-bladder removed, and in October, 1944, was discharged from hospital. Her stools were examined at monthly intervals from October, 1944, until March, 1945, and were consistently positive.

Early in 1945 the desirability of surgical treatment was again pressed on the nurse, and eventually she agreed to have her gall-bladder removed. In April, 1945, she was readmitted to the hospital, and Mr. J. N. Jackson Hartley, senior surgeon at the Cumberland Infirmary, removed the gall-bladder and also the appendix.

Surgical Procedure.—This consisted of cholecystectomy, appendectomy, and freeing of ileum from the old scar. High spinal (percaïne) anaesthesia, with inhalation of cyclopropane, was given. A right paramesial incision from the ensiform process to below the umbilicus was made. The gall-bladder was about one and a half times normal size, and within the gall-bladder there was one stone about the size of the last joint of the index finger. No concretions could be felt in the hepatic and common bile ducts, and the pancreas was not indurated. The cystic duct was isolated and ligated. The gall-bladder was then dissected from the liver and, after tying the cystic vessels, the gall-bladder was removed. Though the appendix did not appear to be abnormal it was removed and the stump invaginated. The last four or five feet (1.2–1.5 m.) of ileum was inspected, but there was no evidence of a Meckel's diverticulum. The abdominal wound was closed in the usual layers without drainage.

Cultures were made from the appendix, the bile, and the gall-bladder wall. Each of these produced a rich growth of *Bact. paratyphosum* B. From the centre of the gall-stone no growth was obtained. Histologically, the gall-bladder showed a chronic