The essential treatment is rest for the limbs. No other treatment is essential, or useful when given without rest. If there be other causes of this familiar syndrome their operation has not so far been demonstrated.

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MISSED CASES OF INFECTIVE HEPATITIS*

EVIDENCE OF LIVER DAMAGE WITHOUT SYMPTOMS AMONG A COMMUNITY AT RISK

BY

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There is a widespread conviction that many cases of infective hepatitis fail to be recognized either because jaundice never develops or because symptoms are so slight that the patient does not seek medical advice. Cases with typical symptoms and abnormal liver function tests but no jaundice are well known to occur, although there is difference of opinion as to their frequency. This problem has been discussed in a separate paper (Pollock, 1945). In many of these so-called "subicteric" cases—particularly among children, in whom the disease is known to be generally milder than in adults—symptoms are minimal; and even in cases that do develop jaundice there are reports of this being the first or only symptom of the attack. Where jaundice occurs the case will not often be missed, whether other symptoms develop or not, but if by any chance it were possible for infection to occur in the absence both of jaundice and of subjective symptoms, the case would almost certainly be missed even under close medical supervision. Such persons would fall into the category of subclinical "ambulant cases" and, although themselves suffering no inconvenience, might be just as capable of transmitting the disease as a fully developed case. Ideally they would be detected by isolation of the infective agent or by specific serological tests; but unfortunately this is not yet practicable. If, however, subclinical infection were associated with some degree of liver damage it might be possible, by the use of a sensitive test of liver function, to obtain suggestive evidence

by investigating a section of a community exposed to risk. Hallgren (1943) has reported raised serum bilirubin values among contacts during an epidemic in a sanatorium, but in view of the wide individual variation known to occur in serum bilirubin concentration it is uncertain how much significance should be attached to his results. In any case, the possibility of liver damage occurring in the absence of symptoms was considered of sufficient epidemiological importance to merit the present investigation.

Methods

For the continued investigation of large numbers of contacts during an epidemic it was necessary to choose a simple liver function test which could be rapidly performed and easily repeated. For this purpose the detection of small quantities of bilirubin in urine by the sensitive method described by Hunter (1930) was considered most suitable. Work (Pollock, 1945; Gellis and Stokes, 1945) on the pre-icteric stage has shown that bilirubin appears in the urine early in the disease, before the serum bilirubin starts to rise, and the test had been found consistently negative in a large series of healthy persons.

The technique of the test and method of collection of samples were slightly modified (Pollock, 1945) in order to increase the sensitivity and allow specimens to be kept for 2 to 3 days before analysis without undergoing deterioration.

Results

A good opportunity for testing contacts occurred at the beginning of 1945 in a residential nursery (Nursery A) for children from 2 to 5 years old. Cases of infective hepatitis had been occurring singly or in pairs among members of the staff at approximately monthly intervals since September of the previous year. The place was excellently run and the standard of hygiene and nursing was high. There was a fairly large turnover of staff, both domestic helps and student nurses, but the population of children (total about 35) remained fairly constant. There was little direct contact between children and the outside population, apart from occasional visits of parents.

On March 11 one of the children (P.H.) became ill and developed jaundice 6 days later. This was the first known case among the children, and it was decided that this would be the most suitable time to begin a mass investigation

of contacts. Accordingly, arrangements were made for the collection of early-morning samples of urine thrice weekly from 17 children (chosen solely on account of their reliability in providing specimens). The investigation went on continuously for 10 weeks, although by this time 4 of the children had left.

FIG. 1.—Nursery A. Serial Hunter's tests for bilirubinuria in child contacts of infective hepatitis.

FIG. 2.—Weekly incidence of cases of infective hepatitis in Nursery A.

* A report to the Medical Research Council.

All but 2 were tested for at least 6 weeks. The results are summarized in Fig. 1. It can be seen that altogether 5 children developed bilirubinuria during the course of the investigation, and in 4 cases tests were positive on more than one occasion. As soon as a suspicious or positive result occurred the child was isolated and kept in bed until 3 successive negative tests had been obtained. A detailed summary of findings in all positive cases is given in the accompanying Table. Unfortunately, in only two instances was

Summary of Findings in those Children in Nursery A who showed Positive Hunter's Tests during the Investigation

Name	Age	Date of First Positive Hunter's Test	Serum Bilirubin		Remarks
			Date	Mg./100 c.cm.	
A.W.	4½	March 19	—	—	No symptoms March 21: Liver not felt; no abdominal tenderness
K.R.	4	„ 21	March 21	0.8 (Direct van den Bergh reaction: positive)	March 20: lethargic; anorexia March 21: Vomited; liver not felt; slight tenderness R. hypochondrium
B.F.	4	„ 26	„ 28	0.4	March 28: nausea and vomiting. T. 100°. Liver not felt; no abdominal tenderness
S.L.	2½	April 11	—	—	No symptoms April 12: T. 100° April 15: Urine "dark"; liver definitely enlarged and slightly tender
J.S.	5	„ 23	—	—	No symptoms April 25: Liver palpable but not enlarged; no abdominal tenderness

it possible to collect blood for the estimation of serum bilirubin. It must be pointed out that the degree of bilirubinuria was relatively slight, since Hunter's test is a great deal more sensitive than most other urine tests for bilirubin, a +++ result corresponding roughly to a just-positive iodine ring test. None of the children ever developed jaundice, but K.R. would probably have been recognized as a "subicteric case," since he was passing very obviously dark urine and had a well-defined clinical attack.

The only child of those being investigated who developed any symptoms without bilirubinuria was P.B., who vomited once on the night of March 31; her temperature was normal and she was perfectly well the next day. Six other children, not in the series, vomited each on one occasion during the period of the investigation; Hunter's tests, performed the following day, were all negative, and with one exception—a boy who developed a temperature of 101.4° and was not well for about a week—recovery was almost immediate. Vomiting is, of course, not infrequently encountered in children of this age, and it is difficult to ascribe much significance to this symptom alone.

It is thus possible to say that suggestive evidence of liver damage and therefore of infection with the agent of infective hepatitis (known to be present in the community) was obtained in 3 cases in the absence of significant symptoms. The most striking cases were S.L. and A.W., both of whom gave repeated unequivocal positive tests over a period of several days without ever developing symptoms. It is unlikely that either would in the ordinary way have been suspected as possible cases, although S.L. was noticed to have passed dark urine on one occasion 4 days after the first positive test; her temperature would not have been taken had she not been under suspicion because of her bilirubinuria, since she appeared perfectly well. In one other case (B.F.) considerable bilirubinuria occurred two days before the onset of symptoms, and in K.R. a suspicious result was obtained one day before the onset.

The sequence of cases in the epidemic is shown in Fig. 2. If all the children who developed bilirubinuria are included as possible cases, it is likely that A.W., K.R., and B.F. were infected at the same time as the first-reported child victim (P.H.)—presumably by one of the two staff cases that occurred in February—and that S.L. and J.S. were secondarily infected from them. The time of occurrence of the symptomless "cases" is consistent with the known incubation period of 20 to 40 days.

No further cases of jaundice have occurred in this nursery up to the beginning of October (5 months after the end of the investigation).

Controls

It was considered advisable to investigate under identical conditions similar communities who had not been exposed to any source of infection for several months. Thirty-two children in two other residential nurseries where there had been no record of jaundice among either staff or children for at least 12 months were therefore tested approximately thrice weekly over periods up to 4 weeks. In 4 isolated cases in one of these nurseries suspicious traces of bilirubin were found, although, so far as was known, all the children were well; but there was no positive result out of a total of 302 tests.

Discussion

It must be admitted that these findings have been obtained in very young children, and at the best remain only suggestive. It is possible that efforts to obtain similar results among an adult community would not be successful. It might also be argued that the children were too young to be capable of complaining of slight subjective symptoms which would certainly be commented upon by adults. But the fact remains that definite bilirubinuria occurred among apparently healthy members of a community exposed to the risk of infection, and such bilirubinuria was not present to any significant extent in similar communities not so exposed. It therefore appears possible that infection with the virus of infective hepatitis may be unrecognized even when special efforts to detect cases are made under close medical supervision.

Summary

Suggestive evidence of symptomless attacks of infective hepatitis among a community of young children exposed to risk of infection has been obtained by the repeated use of Hunter's test for bilirubinuria.

My special thanks are due to Dr. G. Hamilton Hogben, medical officer of health for the borough of Tottenham, and to Miss Moody, matron of Tottenham Residential Nursery, Bengoe, Hertford, without whose willing and efficient co-operation this investigation would not have been possible; also to the matrons and staffs of the nurseries at Abberley House, Shelford, and Kensal House, West Wrattling, who most generously helped in collecting control specimens from children under their care.

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AMPUTATIONS, RE-AMPUTATIONS, AND PENICILLIN

BY

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This communication is based on some 102 amputations and re-amputations, 90 of which were performed during a 6-months period at the Ministry of Pensions Hospital, Chapel Allerton, Leeds. There were 19 primary amputations and 83 re-amputations; amputations of digits and trimming operations on soft tissues are not included.

Twelve cases operated on previously to the 6-months period were selected as cases which would have been suitable for post-operative penicillin had it been available. The majority of the 83 re-amputations were performed on patients whose original amputations had been carried out under active-service conditions, where the primary consideration was to save life. All the re-amputations were necessary for limb-fitting purposes. Some of these, however, had undergone primary amputations in ideal hospital conditions, only to be subjected to re-amputation because the original stumps were unsuitable for the fitting of artificial limbs. The reason for this is probably the retention in most textbooks of operative surgery of descriptions of classical amputations which should be revered for their antiquity rather than practised by surgeons. An invaluable book on the