INOCULATION HEPATITIS

BY

H. MALMROS, M.D.*Physician-in-Chief***O. WILANDER, M.D.***Head of the Clinical Laboratory*

AND

B. HERNER, M.D.*(From the Central Hospital, Örebro, Sweden)*

As is well known, the name "homologous serum jaundice" is still often employed, though it is in some way misleading. The term "jaundice" ought to be replaced by "hepatitis," as the disease is due to a virus infection that produces the same symptoms as common epidemic infective hepatitis. The virus is already present in the blood during the pre-icteric period and can be transferred not only with the serum but, of course, also with plasma and whole blood. The term "haematic" or "haematogenous" hepatitis has therefore been proposed. As the virus which produces this disease is not completely identical with that responsible for epidemic infectious hepatitis, the distinctive terms hepatitis of type A and B respectively (MacCallum) or X and Y disease respectively (Beattie and Marshall) have also been suggested.

It may appear to be of no consequence which designation is chosen. This is by no means the case, however, for the power of language over thought is such that we are apt to obtain a fallacious conception of the nature and paths of infection of the disease by employing a term that has reference to only one of the many spreading possibilities of the infection. Nor should we class the disease as B or Y, for such a designation may easily occasion confusion with A or X and, moreover, is quite certainly meaningless. In the Scandinavian literature the term "inoculation hepatitis" is used. As will be shown below, this is a fully adequate expression and also an appropriate name, since it warns physicians and other hospital staff of the risk of transferring the disease by inoculation from one patient to another.

Early Observations on Diabetic Patients

As early as 1925, at a Scandinavian congress in Stockholm, one of us (Malmros) drew attention to the risk of infection to which patients were exposed when blood samples were taken. During the year 1923 Malmros had an opportunity of observing an epidemic of hepatitis among diabetic patients who were being attended in the Medical Clinic of Lund. He was then able to establish the fact that the infection was probably transmitted at visits of the patients to the laboratory, for cases also occurred among patients who had not been admitted to hospital but had incidentally visited the laboratory for blood tests. For such cases as well as for patients who had fallen ill after being discharged from hospital the period of incubation could be estimated at about three months. Most of the patients had not been treated with insulin, and hence it may be taken that the insulin injections had not played any part in the origin of the disease. The patients had not received blood transfusions or other injections either. Altogether the epidemic embraced 34 cases, 28 of which were diabetics. Among the population in general there was no extensive hepatitis epidemic at this time.

Transference of Infection in Blood-sampling

After exhaustive studies of the various possibilities for transmission of the infection we finally came to the decision that the virus of the disease had been unintentionally trans-

ferred by inoculation from one patient to another in connexion with samplings for the blood-sugar analyses. For these analyses capillary blood was used, which was obtained by pricking the finger or the lobe of the ear with a "blood-gun." The same instrument had been employed on several patients and had only been hastily cleaned by wiping it with an ether swab. Three months after the attention of the laboratory staff had been drawn to the risk associated with this unsuitable technique the epidemic came to an end.

Amassed cases of hepatitis in diabetics have subsequently also been described by other authors (Steinitz, 1931, 1932; Bade, 1936; Graham, 1938; Stockinger and Wenzel, 1938; Ducas and Uhry, 1939; Selander, 1939; Vannfält, 1944; Odin, 1945; Droller, 1945). Most of these have come to the conclusion that the cause of hepatic cases among diabetic patients is the transmission of the infection in connexion with the blood-sampling. Of particular interest are Selander and Odin's observations of the occurrence of hepatitis among patients who had been attended earlier in hospital. In the city of Gothenburg, in Sweden, all cases of jaundice have been notifiable since 1901, and this has enabled a good survey to be kept of the epidemiological situation during the past years. In Selander's material, which comprises 960 cases from 1924 to 1938, there were 274 "return" cases—i.e., patients who had been attended in hospital the year immediately before contracting hepatitis. Of this number 47 were diabetics. The period of incubation for these return cases was generally two to three months. The risk of contracting hepatitis was estimated to be 40 times greater for patients who had been in hospital than for the rest of the town's inhabitants. After Odin had carried rigorous prescriptions into effect as regards sterilization of the syringes and lancets used for blood-sampling the number of return cases diminished considerably; indeed, they almost terminated completely.

It is accordingly clear that the epidemic as well as the sporadic appearance of hepatitis can be due to transmission of the virus from one person to another in connexion with interventions of various kinds undertaken by physicians and other members of the hospital staff. We have to reckon with there being risk of inoculation hepatitis associated with: (1) serum, plasma, and blood transfusions; (2) protective inoculations for which serum, lymph, or some other biological material derived from human beings is used; (3) intravenous injections if a syringe earlier used for other patients is re-used without proper sterilization; (4) intramuscular injections, which may also constitute a risk in that blood or tissue fluid that is under a certain pressure can produce a reflux through the injection needle into the syringe; (5) blood-sampling, whether of venous or of capillary blood.

A Special Sampling Instrument

That there is a risk of transmitting the virus of hepatitis by the use of a so-called blood-gun that has not been carefully sterilized after each use is evident from the above-mentioned hepatitis epidemic in Lund. Quite naturally it is not only diabetics that are liable to be infected at blood-sampling. Patients are also exposed to this risk at so simple and common a test as a haemoglobin determination. Experience has shown that it is very difficult to achieve a fully reliable sterilization of blood-guns. Washing with ether, alcohol, or other disinfectants is not sufficient. For this reason we have tried out a special sampling instrument into which a fresh sterile needle is fitted for every patient (see Fig. 1). The instrument consists simply of a holder for Miller needles like that used by dentists in the treatment of the root-canal. Gramophone needles are used instead of the long slender Miller needles. Flat needles are the best, but the ordinary round ones will also do. After use they are washed in alcohol and dry-sterilized.

Mendelssohn and Witts (1945) have made a close study of the risk of spread from venepuncture with syringes that are washed but not sterilized. With a syringe containing methylene blue they punctured a rubber tube through which water was running, pointing the needle in the same direction as the water was flowing. They were able to show that as soon as the negative dynamic pressure caused by the flow of water becomes higher than the hydrostatic pressure the contents of the puncturing-syringe are drawn by suction into the water flowing through the rubber tube, whereupon the water is stained blue.

As it seemed to us highly desirable for this important problem to be further elucidated, we repeated Mendelssohn and Witts's experiment, but altered the experimental conditions somewhat to bring them into closer accord with the physiological conditions. By direct measurement we convinced ourselves that following constriction the venous pressure can rise to 1,200 mm. H₂O. When the tourniquet is loosened the blood starts to flow and the venous pressure falls rapidly. Mendelssohn and Witts did not take this into account in their model-experiment, but on the whole kept the same hydrostatic pressure during the entire experiment.

In our experiment we employed an approximately 1½-metre-long narrow transparent plastic tube, which was filled with water through a funnel. At the beginning of the experiment the outflow was closed with a clamp and the other end of the tube was raised to a height of about 1,200 mm. The horizontal part of the tube was punctured with a needle fitted to a sedimentation syringe of Westergren's model con-

FIG. 1

taining methylene-blue solution instead of sodium citrate. The clamp was thereupon opened to allow the water to flow through the tube, and the hydrostatic pressure was simultaneously reduced to normal venous pressure (40–80 mm. H₂O) by lowering the funnel. With this experimental arrangement we were unable to demonstrate any suction of methylene blue into the water from the syringe.

However, as we considered it to be theoretically possible that Mendelssohn and Witts's interpretation was correct in spite of this, we repeated the experiment with a somewhat altered technique and then used a more sensitive indicator than methylene blue. The experiment was carried out in a dark room in which the source of light consisted of an ultra-violet lamp with a black filter (wavelength c. 3,650 Å). A 20% sodium fluorescein solution was drawn into the syringe. Under ordinary light this solution has the appearance of a brown-coloured fluid. Under ultra-violet light,

on the other hand, even the smallest trace of it when mixed with water gives an intensely bright yellow colour that can be distinctly seen even through a plastic membrane. Before the puncture a needle (previously never used) was fitted to the syringe. With these experimental dispositions we succeeded in showing that a few seconds after water started to flow through the tube a stream of fluorescein solution issues—like a streak of fire—from the tip of the needle (see Fig. 2). Alteration of the hydrostatic pressure by alternately

FIG. 2

raising and lowering the funnel disclosed that the inflow from the syringe sometimes ceased and then increased again when the pressure conditions were reversed.

With the aid of fluorescein solution we have also been able to show that in certain cases fluorescein is forced out of the syringe through the whole needle when the latter is fastened to the syringe. In the ultra-violet light the small drop of fluorescein is then seen to gleam like a glittering pearl in the outlet of the syringe-needle. We were able to produce this phenomenon in only a few solitary instances, and the condition necessary for its appearance was that the needles had been sterilized by boiling so that they contained a little drop of water when they were fitted into the syringe. However, dry sterilization of the syringe-needles does not afford protection against suction as a result of a negative dynamic pressure, for even in those cases in which we made use of entirely dry needles we obtained a distinct fluorescein streak in the flowing water.

Comment

These experiments make it obvious that there is a risk of transferring the infection in all those cases in which inefficiently sterilized syringes are employed for venepuncture. This established fact plainly involves serious consequences, for the great majority of physicians have hitherto used the same syringe for many patients—e.g., at blood-samplings for the sedimentation test. If we wish to ensure that our patients are not exposed to any unnecessary risks we must make it clear to ourselves and to our nurses and other hospital staff that infection is liable to be transmitted as soon as we use a non-sterile syringe. In times of peace the provision of a satisfactory number of syringes is merely a financial problem that ought not to be allowed to stand in the way of securing for our patients an effective protection against a serious and completely unnecessary disease. As a matter of fact, with some training it is possible in many cases to perform venepuncture solely with an acupuncture-needle without using syringes and to let the blood drip into a test-tube.

Summary

Risk of inoculation hepatitis is present at: (1) serum, plasma, and blood transfusions; (2) protective inoculations with human serum or lymph; (3) injections, intravenous as well as intramuscular, unless sterile syringes are used; (4) blood-sampling, whether of venous or of capillary blood.

A so-called blood-gun is extremely risky to use, being very difficult to sterilize. It ought preferably to be replaced by a needle-holder and exchangeable gramophone needles.

By the use of sodium fluorescein solution under ultra-violet light a model-experiment has been conducted and has shown that there is risk of infection transmission if non-sterile syringes

are used for venepuncture. At blood-sampling for the sedimentation test we must also calculate with the presence of this risk.

The risk of infection can be eliminated in two ways: (1) by the use of sterile needles alone without syringes at venepuncture; (2) by the provision of a sufficient number of syringes to enable a fresh sterilized instrument to be used for every patient.

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SYRINGE-TRANSMITTED JAUNDICE

AN INQUIRY AND A PLEA

BY

R. S. MORTON, L.R.C.P.&S.Ed.

Assistant Medical Officer, Newcastle General Hospital

At least two articles have been published demonstrating the inadequacy of sterilization technique coincident with a high incidence of jaundice in V.D. clinics. Three convincing series of observations (notably that of Laird, 1946) show that adequate sterilization and supervision of intravenous technique result in a fall in the percentage of syphilitics developing hepatitis while under treatment.

The present investigations were conducted in a V.D. clinic where sterilization and intravenous technique were believed to be adequate and yet the incidence of hepatitis was high. The period reviewed was April 1 to Sept. 30, 1947; only male patients receiving intravenous arsenicals were investigated. Results were as follows:

	No. of Cases	No. Previously Under Treatment	No. of New Cases
Investigated	338	173	165
Observed for 6 months	242	135	107
Developing hepatitis	64 (26.4%)	28 (20.7%)	36 (33.6%)

"New" cases indicate those coming under intravenous arsenical therapy for the first time.

It will be appreciated that at April 1 a certain number who should have been still "under treatment" were lost to the series on account of hepatitis, with subsequent suspension of arsenicals. This could explain the discrepancy in the percentages 20.7 and 33.6.

Three of the "previously under treatment" cases of jaundice occurred in patients transferred from other clinics for continuation of treatment; all three developed jaundice within three weeks of their first attendance after transfer. This very short incubation period makes it unlikely that they received their infection at this clinic.

Only one death occurred among the 338 cases—from agranulocytosis believed due to arsenicals. The patient developed pneumonia with slight icterus and bile in the urine. This case is not included among those developing hepatitis. Patients receiving penicillin or bismuth and routine blood tests only were not included in the investigations.

Sterilization was conducted by boiling in a small electric sterilizer, which was also used for the blood-collecting and

bismuth syringes. Boiling took place in a room separate from the medical officer's examination and treatment room; the process was therefore not under his easy control. About fifteen syringes of the numbered "vim" pattern were available for intravenous therapy. For boiling, the syringes were dismantled and wrapped in gauze, and it was noted that they were not always completely submerged in the boiling water. Boiling times varied between 10 and 30 minutes. On completion of boiling the wrapped syringes were laid on a tray ready for use. Needles were similarly boiled and placed in a dish of distilled water. Preparation of the injection material in a gallipot was carried out by the male orderly, using distilled water from an upturned flask. The charged syringe was handed to the medical officer, who gave the injection. The syringe was then returned to the orderly, who washed it out with tap-water and placed it in the "dirty" bowl; this bowl contained distilled water, changed daily, and it was the practice to draw a few millilitres of the water into each syringe as it was placed in the bowl. Before wrapping a syringe for boiling, the water in it was ejected into the bowl again. No antiseptics were used at any stage of the procedure.

Preparation of intravenous material and charging of syringes was carried out on a bench behind the medical officer while he was examining patients and/or reading and writing case notes. It was observed that at the end of almost every session investigated the number of syringes in the "dirty" bowl did not correspond to the total number of injections given during the session. It was noted also that this occurred irrespective of the medical officer or orderly on duty and irrespective of any combination of the same.

Specimen observations are as follows:

Day 1: Morning Session

8.30 a.m.—Tray: Syringes Nos. Z535, 843, 0124. "Dirty" Bowl: Syringes Nos. 330, 7, 140, X130, Record.

9.15 a.m.—All syringes were boiled for 15 minutes.

10.00 a.m.—Session started, running to 12 noon.

12.15 p.m.—Tray: Syringes Nos. 843, 330, 0124, X130, 140, Record. "Dirty" Bowl: Syringes Nos. 7, Z535.

No boiling took place during the session. Seven intravenous injections were given and only two syringes, 7 and Z535, were used.

Day 2: Morning and Afternoon Sessions

8.30 a.m.—Tray: Syringes Nos. 843, 567, Z535, 330, Record, X130. "Dirty" Bowl: Syringes Nos. 140, 7, 0124.

9.15 a.m.—Syringes Nos. 0124, 140, and 7 were boiled for 20 minutes.

10.00 a.m.—Session started, running till 12 noon.

12.15 p.m.—Tray: Syringes Nos. 843, 567, Z535, 330, Record, X130. "Dirty" Bowl: Syringes Nos. 140, 7, 0124.

No boiling took place during the session. Five intravenous injections were given and only three syringes, 140, 7, and 0124, were used.

7.15 p.m.—Despite further intravenous therapy the arrangement at 12.15 p.m. still existed. Except for the 9.15 a.m. boiling, no boiling took place during the day.

Day 3: Morning and Afternoon Sessions

8.30 a.m.—Tray: Syringes Nos. 843, 567, Z535, 330, Record, X130. "Dirty" Bowl: Syringes Nos. 140, 7, 0124.

9.15 a.m.—Syringes Nos. 140, 7, 0124 were boiled for 15 minutes. No further boiling during the day.

7.15 p.m.—Tray: Syringes Nos. 843, 567, 7, Z535, Record. "Dirty" Bowl: Syringes Nos. 140, X130, 0124, 330.

Ten intravenous injections were given during the day, and only five syringes, 140, X130, 0124, 330, and Record, were used.

It was therefore obvious that syringes were used and re-used without adequate sterilization. Such routine was contrary to standing instructions.