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The first episode of dialysis-associated hepatitis in Edinburgh occurred in 1966 when two patients were affected. At that time measures were introduced which were essentially the same as those recommended in 1968 by the Public Health Laboratory Service working party on haemodialysis units (1968) and no further cases arose until June 1969. Between June 1969 and August 1970 26 patients on dialysis in Edinburgh developed clinical hepatitis, and seven died as a direct result of their illness. Two home contacts of these patients and 12 staff contacts also developed hepatitis, and 4 previously healthy young people, 2 transplant surgeons and 2 laboratory technicians, died in consequence.

The time course of the outbreak in the patients and their contacts is shown in Figure 1. At the end of April 1969 the first patient was given one unit of blood from a donor who was incubating hepatitis. The patient developed hepatitis in June, 51 days after the transfusion, and the second patient developed hepatitis 58 days after the onset of hepatitis in the first patient.

Figure 1. Dialysis-associated hepatitis. Edinburgh 1969/70
Both patients had been dialysed on Kolf machines with disposable coil dialysers and were isolated over the period of their acute illness. After clinical recovery they were treated in the newly-built chronic dialysis area using Kolf dialysers and Dylade machines with the other patients.

After an interval of 90 days, two more patients became ill and the outbreak became explosive after December 1969. Dialysis techniques and codes of practice which were under continual review were further revised in February 1970 with a reduction in the incidence of hepatitis in the patients, and further measures, which included closing the chronic dialysis area to new patients, were introduced in June 1970. There have been no further cases of hepatitis among patients dialysed in the regular dialysis area since August 1970.

Tests for Australia (HA) antigen were positive in the acute stage of the illness in every dialysis patient who developed clinical hepatitis, with the exception of the first two. In striking contrast to the experience of other units, all patients have now become negative, with the exception of one patient who had a successful transplant and is on immunosuppressive treatment. No patient on dialysis has become Australia antigen positive without developing clinical hepatitis. In contrast, only 5 of the 14 contacts who developed hepatitis were Australia antigen positive, and these included the most severely ill. The others were negative even during their acute illness although the majority had antibodies to Australia antigen as detected by haemagglutination inhibition. None of the other 100 contacts working in the Medical Renal Unit have become positive for Australia antigen or antibody despite regular screening.

The peak incidence in the contacts followed the peak incidence in the patients by an interval of 2 to 3 months. This is in good agreement with the incubation period of 50 to 70 days when this could be identified in individual patients and contacts, and also with the interval between groups of patients contracting hepatitis.

Gamma globulin was given to the first patient in a dose of 6g and in February was given in a dose of 1.5g to all remaining patients and to all new patients starting dialysis. Contacts were given gamma globulin in a dose of 1.5g as soon as possible after a mishap. There is no statistical proof that gamma globulin prevented hepatitis or reduced mortality, but numbers are small.

In order to show that hepatitis is not confined to dialysis units, we have included data on the incidence of hepatitis in the general hospital population in Edinburgh. Of the 12 staff contacts, 2 were transplant surgeons, 2 laboratory technicians, 3 dialysis technicians and 5 nurses. A clear relationship with one or more infected patient could be identified in all but one.

Table I shows the hospital area where contacts occurred and the most
<table>
<thead>
<tr>
<th>Area where contact occurred</th>
<th>No</th>
<th>Route of transmission</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Dialysis area</td>
<td>2</td>
<td>Needle Accident</td>
<td>3</td>
</tr>
<tr>
<td>General Ward area</td>
<td>4</td>
<td>Blood in Face</td>
<td>3</td>
</tr>
<tr>
<td>Operating Theatre</td>
<td>1</td>
<td>Cut hand</td>
<td>1</td>
</tr>
<tr>
<td>Laboratory</td>
<td>2</td>
<td>Operation</td>
<td>1</td>
</tr>
<tr>
<td>Transplant Unit</td>
<td>3</td>
<td>Unknown</td>
<td>4</td>
</tr>
</tbody>
</table>

likely route of transmission when this could be identified. The Medical Renal Unit and chronic dialysis area where the outbreak started is situated 3 miles away from the Transplant Unit and the units are run by different staff. The Transplant Unit became involved through the transfer of patients who were incubating hepatitis although Australia antigen negative at the time. There can be little doubt that in this outbreak transmission occurred by the inoculation of blood or infected excreta through breaks in the skin surface or by splashes on to mucous membranes and these should be prevented if skin and mucous membranes are adequately protected. Despite the much greater exposure of staff to infected patients, only 2 of the 12 contacts were infected in the chronic dialysis area where precautions were much more stringent than elsewhere in the hospital, and we would now consider even these to be preventable.

Precautions against the spread of infection between dialysis patients included the functional division of the dialysis area between infected and non-infected patients, the provision of separate changing and toilet facilities, the use of disposable utensils and other restrictions on the consumption of food within the unit.

In a dialysis unit blood-borne transmission between the patients is most likely to take place through the dialysis equipment. Before February 1970 14 Kilms had been used freely between all patients in the chronic dialysis area, but in February Kilms were allocated to individual patients and used by no-one else. New ones were purchased and existing Kilms sanitised by exposure to steam at 100°C. After each dialysis the Kil boards were scrubbed in a detergent solution containing hypochlorite, the dialysers from patients with hepatitis being treated separately and washed in a different sink. After reassembly all dialysers were sterilised by exposure to 2% Glutaraldehyde for 1 hour.

Despite these measures new cases of hepatitis continued to appear, but at a reduced rate.

At the beginning of March it was noted that in one machine the plastic tube behind the display panel connecting the venous pressure manometer to the external port was contaminated with blood, and although this seemed at the time to be an unlikely source of infection all tubes were changed and staff
alerted to the danger of further contamination. From April machines were numbered and a record kept of the machine used by particular patients. It should be pointed out that contamination of the venous pressure gauge in this way is possible with most types of monitor that are available.

Figure 2 shows how machines 2 and 14 could be implicated in the transmission of hepatitis from 3 patients, including 2 who were Australia antigen positive at the time, to a further 4 or 5. One of these patients was not clinically ill or Australia antigen positive, but showed a rise in SGPT to 540 units/ml.

In June additional measures were taken as shown in Table II.

Table II. Measures to prevent transmission via machines

1. Venous pressure gauges changed, tubes renewed, external port cleaned with Glutaraldehyde.

2. Dialysate tubing inside machine sterilised by
   (a) Diversol and Pyroneg
   (b) Cidex
   (c) Heat - 90°C for 15 min x 2

3. Dead space - 30ml - between venous bubble trap and venous pressure gauge, changed with each dialysis. NB Interim measure.

4. Each machine allocated to 3 named patients.

The last two patients became ill with hepatitis in August 1970 from contacts made before these measures were taken. In the last ten months, no other patient in the chronic dialysis area has developed hepatitis, and no other contact has become infected. The unit has only in the last month been evacuated of patients who have had hepatitis, the majority into the home, and the remainder to a small separate dialysis area.
Table III. Measures to avoid spread to staff

1. Meticulous personal hygiene
2. Protective clothing
3. Extreme care with needles
4. Train patients to do own needling
5. Codes of practice for unit and laboratories
   for handling blood samples, etc

Table IV. Measures to avoid infection of patients

1. Individualise dialysers, or use disposable dialysers
2. Limit use of dialysate supply and monitoring systems, and
   prevent contamination
3. Fewer patients on hospital dialysis, more on home dialysis
4. Remove infected patients from unit — establish separate unit
5. Prevent reintroduction of infection
   - reduce transfusion of blood
   - screen blood, patients, transplanted kidneys
   for Australia antigen

The precautions that we would recommend in the light of our experience are
summarised in Tables III and IV. The use of meticulous personal hygiene,
protective clothing, and extreme care with needles, the training of patients
to do their own needling and the establishment of codes of practice for the
unit and laboratories for handling blood samples and for dialysis procedures
should prevent the spread of infection to the staff. The patients should be
protected from hepatitis by the measures directed against the dialysis equip-
ment that we have described and by reducing the number of susceptible
patients on hospital based dialysis. However, the only ultimate safeguards
are to remove infective patients from the unit entirely, and to prevent re-
introduction of infection (Table IV).

ACKNOWLEDGMENTS

We should like to acknowledge the help of Dr J D Cash and Dr P C Das of
the Blood Transfusion Service for the provision of stored samples of patients’
sera and for retrospective analysis and for the testing of Australia antigen
in the early days of the outbreak.

REFERENCE

British Medical Journal (1968) 3, 454-460. Infection risks of haemodialysis
- some preventive aspects. A report to the Public Health Laboratory
Service by the working party on haemodialysis units.
OPEN DISCUSSION

W DUTZ (Berlin, DDR, Chairman): The news of the Edinburgh outbreak has gone over the world and has alarmed every dialysis centre. This paper is now open for discussion.

M McGEOWN (Belfast): In Belfast, Northern Ireland, we have been free of hepatitis in the renal unit. This has been more our good fortune than anything else, though we have had Au antigen testing through the Colindale Public Health Laboratory in London since 1968. However, in our community both epidemic hepatitis and sporadic cases of hepatitis are common, and it is clear that hepatitis within renal units occurs in populations where the outside population is already infected with hepatitis. It is clear that the Edinburgh epidemic arose from a unit of blood which was contaminated, and also the earlier epidemics in Great Britain at Liverpool and Manchester appeared to occur in a community in which there was a high level of hepatitis. With these considerations in mind, therefore, we set up a working party on hepatitis in the community in Northern Ireland at the beginning of this year.

The brief of this working party was to study the spread of hepatitis within the community, within the renal unit and also within the laboratory. Here, we were fortunate to have advice from Professor Marmion and the experience of the Edinburgh epidemic to guide us. At the meeting we have already held, we uncovered a number of new problems of which we were not aware. First of all, hepatitis notification is very incomplete; the statutory regulations required the notification of cases of hepatitis occurring in epidemic form, but did not require the notification of hepatitis which occurred following blood transfusion. We have been able to redraft the regulations already. We found there was widespread alarm amongst the laboratory staff lest they would be contaminated with renal unit blood specimens, and this was carried to ridiculous lengths. We were able to institute sensible precautions and found that in the laboratory (particularly the biochemical laboratory) there was very careless handling of all specimens, and that no care was taken in many of the places where workers might become contaminated with blood. We have set up local Au antigen screening for hepatitis and have found already that Au antigen occurs in the hepatitis that is occurring outside the renal unit. There is a general lack of isolation facilities, and indeed cases were not isolated previously to the setting up of this working party. There are legal implications concerning the spread of hepatitis to staff and the spread of hepatitis to relatives of home patients, which need to be clarified.

Finally, it is essential at all levels where jaundiced patients occur, that there is a need for continuous vigilance on the standard of personal hygiene and precautions.
F PARSONS (Leeds): I don't think, Dr Bone, that you have explained the whole position. I'd like to know your total death rate. As far as the Registration Committee are concerned, I think this is a problem that's going to affect everybody. I would like to know how many patients presenting in terminal renal failure you were unable to take on to treatment because your unit was closed for accepting new patients? I think this is a very, very important point; you are a closed community in South East Scotland, and as far as I am aware have no other dialysis facilities other than in Edinburgh. When we are discussing mortality, we must look at the community as a whole, not just the patients in your unit. According to the results you have just given, your returns for the number of cases of staff with hepatitis to the Registration Committee were quite incorrect. As far as I understand from your returns, you only took on five new patients last year. What happened to those presenting in terminal renal failure that you did not take on?

BONE: Well, in answer to your first question, the death rate from hepatitis that I quoted was for patients who died as a direct result. Now other patients who had had hepatitis did die, but with hepatitis perhaps as a secondary or contributing cause. In terms of the numbers who were returned to the central data collecting area, our returns were for the medical renal unit in the Royal Infirmary alone and not for the other unit at the Western General Hospital (the Nuffield Transplantation Unit) who made a separate return. The area that we closed to the admission of patients was the chronic dialysis area, that is, the newly built ten bedded area where the patients with hepatitis were still being dialysed. We fell back on the facilities we used before this unit was built, and continued to take on patients for dialysis, but these patients were dialysed in side wards, in cubicles, in any space that could be found. As far as I am aware, there were few patients, perhaps one or two, who would normally have been dialysed and who were not treated by dialysis. Another way in which patients with terminal chronic renal failure were handled was by direct transplantation; some four or five patients were transferred directly to the Nuffield Transplantation Unit, and either had a short period of dialysis there, or were transplanted directly without previous dialysis. It is interesting to note that a number of these patients have done very well indeed. Two patients were discussed with other units. We were fortunate to have the help of Dr John Moorhead for one patient. He very kindly trained this patient in dialysis procedures, established her shunt and the like, and returned her to Edinburgh for home dialysis where she is still being treated. Professor Kerr at Newcastle accepted the other patient from us for treatment by renal transplantation.

J S CAMERON (London): I would like to make a comment and ask a number
of questions of Dr Bone, the comment being that we, at Guy’s Hospital in London, have the unenviable distinction of having the fastest growing hepatitis epidemic in the world. We have almost 100 cases, of whom two-thirds have been in general staff all over our hospital — including laboratory and theatre staff — as well as those intimately concerned with the ward and unit care of the patients. All this in spite of adopting most of the precautions that have been so far discussed. Therefore we are very concerned about this problem. My questions are, first, what method of Australia antigen testing are you using of the three or four available?

BONE: Now we are using the immunoelectrophoretic method. At the start of the outbreak we were using just straightforward double diffusion on agar plates.

CAMERON: Second, as was mentioned by Dr McGeown, have you had any spread to relatives of either staff or patients with hepatitis?

BONE: The two home contacts were the wife and son of one of our patients. There has been no spread from infected contacts to other members of their families.

CAMERON: To comment on Dr Parson’s point on consequent death rate, we ourselves have had to take our intake down from one per week to none per year. How many patients died because either you refused to take them on because they were Au antigen positive at screening, or because when their transplants failed, or in other circumstances, you were unwilling to readmit them to dialysis in the presence of a positive test? We have been placed in this unfortunate position now on several occasions.

BONE: We haven’t had to encounter this problem, fortunately. The policy for a patient who requires dialysis and is antigen positive, or who requires dialysis returning from transplant and is positive, is to transfer them straight to the separate unit — what we call the 'yellow' unit — for infected patients, where there are two patients surviving from our epidemic who are being dialysed. This acts as a back-up facility for the home dialysis patients who have had hepatitis, as well as for the problems you mention.

CAMERON: Finally, would it be fair to say that the existence of such a back-up, separate dialysis facility for 'yellow' patients, with as comprehensive care as possible within those four walls, is an essential feature of the care of a unit dealing with Au antigen positive patients?
BONE: I would agree with that.

W DUTZ (Berlin, DDR, Chairman): Would you please allow me one remark for myself? Hitherto we have had only a few cases of hepatitis in our dialysis centres, either among patients or among staff. There is one interesting feature: we analysed 16,000 blood donors in the Berlin blood bank, and found 67 Au antigen positive donors, that means 0.4%. A significant sample of these were thoroughly investigated clinically, including liver biopsy, and there were signs of chronic hepatitis in 36%. It is essential, I think, to omit every blood donor who is Australia antigen positive.