Important events in dialysis in Edinburgh

The Edinburgh hepatitis outbreak

There was a period of a high prevalence of viral hepatitis in UK dialysis units, the first in Manchester in 1965. Soon after the new MRU opened in Edinburgh in June 1969, the first case occurred in Edinburgh.

The index case

In April 1969, a CRF patient was transfused with one unit of blood that was incubating hepatitis. 51 days after the transfusion (June, 1969), the patient developed hepatitis. 58 days after the onset of hepatitis in the first patient, a second patient developed hepatitis. (Bone et al, 1971). 2 more patients developed hepatitis after an interval of 90 days. The outbreak became severe after December 1969.

Mechanism thought to have caused outbreak

The CRF patient who got infected through a blood transfusion was dialysed. The proportional pumping dialysis machines used in the MRU building at the time had limited safety features. Blood went up one of the lines from the patient to the machine, and the venous pressure gauge recorded the pressure in the line returning blood to the patient. It was thought that a small volume of the infected blood contaminated the venous pressure gauge. The gauge, being a permanent feature of the dialysis machine, was not changed with the blood lines. When the next patient was connected to the dialysis machine with new lines, the infected blood was passed into the patient via the new lines.

The areas within the hospitals where contact may have occurred were the chronic dialysis area (MRU), general ward area, operating theatre, the transplant unit and the laboratories. Likely routes of transmission included the dialysis machines, hypodermic needle accidents, cuts in the hand and blood contacting the breached skin surfaces and mucous membranes. The handling of contaminated faeces and

urine, leaking specimen containers or aspiration of infected blood into the mouth while using a pipette are also possible routes of infection (Marmion & Tonkin, 1972).

The MRU at RIE and the Nuffield Transplantation Surgery Unit at the Western General Hospital (WGH) in Edinburgh were seriously affected despite taking all precautions then known against risks of infection. There were a total of 40 cases of clinical hepatitis in Edinburgh between June 1969 and August 1970, including 26 patients, 2 home contacts and 12 members of staff (surgeons, nurses, technicians). Of these, 7 patients, 2 laboratory technicians and 2 transplant surgeons died as a direct result of the infection (Bone et al, 1971). All the dialysis patients who developed clinical hepatitis tested positive for the Australia antigen in the acute stage (Bone et al, 1971).

“I have vivid memories of new patients who started dialysis and 4 months later, got infected and died. Only later on that year was the mechanism of spread identified.” (Dr R Winney)

Other renal units also had severe outbreaks of hepatitis. The unit at Guy’s hospital in London closed after 69 cases of hepatitis occurred (including 32 staff) (BMJ, 1970). The units at Charing Cross in London, Birmingham and many other areas across UK were also affected. The highest incidence of death as a direct result of the hepatitis infection in the UK was in Edinburgh (Rosenheim report, 1972).

Outbreak	Date	Patient cases	Contacts cases	Staff cases	Total cases	Patient death	Staff death	Total death
Manchester	1965/66	5	–	11	16	–	3	3
Liverpool	1966/71	15	7	33	55	–	–	–
Charing Cross I	1966/67	15	–	–	15	–	–	–
Charing Cross II	1968/71	64	–	–	65	–	–	–
Birmingham	1967/71	21	4	12	37	–	–	–
Newcastle	1969/71	4	1	–	5	1	–	1
Royal Free	1969/70	3	–	8	11	–	–	–
Hammersmith I	1969/70	6	–	1	7	3	–	3

Hammersmith II	1971	6	–	2	8	–	–	–
Edinburgh	1969/71	18	2	8	28	8	3	11
Guys	1969/71	33	14	42	89	–	–	–
Cardiff	1969/71	16	1	4	21	–	–	–
TOTAL		206	29	121	357	12	6	18

Table showing 12 outbreaks (2 or more cases) of hepatitis in British regular dialysis and renal transplantation units by September 1971 (modified from the Rosenheim report, 1972)

The hepatitis outbreaks led to the establishment of an advisory group to the Department of Health and Social Security, Scottish Home and Health Department and the Welsh Office. Lord Rosenheim, the consultant physician of the University College Hospital, chaired the committee. Professor Sir Michael Woodruff and Dr James S Robson were among the 15 members of the advisory group who came from around the country. The committee included physicians, surgeons, a sister and a matron. They produced a set of recommendations aimed to minimise the spread of hepatitis. Lord Rosenheim wrote: “Anxiety about the infection is understandable, but there are no grounds for a negative or defeatist attitude… I hope that all concerned will accept the recommendations and modify their practice in accordance with the suggested codes and that such positive action may lead to the prevention of further outbreaks and alleviation of anxiety.” (Rosenheim report, 1972)

Some conclusions of the Rosenheim report

- Regular dialysis and renal transplantation are established and effective forms of treatment
- The form of hepatitis is usually but not invariably associated with the Australia antigen or its antibody or both
- Control of infection is most likely to be achieved by comprehensive measures based on well-recognised principles. A code of practice is recommended

Recommendations:

- Blood transfusions should be minimised for patients with chronic renal failure; only blood screened as negative for the Australia antigen and its

antibody should be used
- Patients and staff in regular dialysis and renal transplantation units should be regularly screened for evidence of infectivity
- Patients with chronic renal failure should be screened prior to admission to regular dialysis units
- Movement between units should be controlled; patients from overseas who cannot be fully assessed before admission should not be admitted
- Early discharge to home dialysis will minimise the risk of hepatitis
- Present dialysis equipment may not be entirely free from the risk of transmitting infection.
- Research into the design of equipment is being pursued and should continue. Disposable dialysers should be used for infective patients
  the workload in regular dialysis and renal transplantation units should not be allowed to reach such a level that full precautions cannot be taken
- Laboratory staff dealing with specimens from regular dialysis and transplantation units must take special precautions and be fully briefed
- All regular dialysis and renal transplantation units should co-operate with the Public Health Laboratory Service in the study of epidemiology
- Hospital laboratories should report all findings of Australia antigen to the Public Health Laboratory Service

Hepatitis outbreak containment measures in Edinburgh

The crucial modification in Edinburgh to stop spread of hepatitis was the use of a venous pressure isolator, a “membrane” which acts as a protector of the gauge, so that patient’s blood no longer went directly into machine but went onto a filter first. The length of the tubing leading to the gauge was also doubled, minimising potential contamination.

For 6 months new patients were not accepted into the MRU of RIE or the Nuffield Transplantation Surgery Unit. Ward 44 was used for HD of hepatitis patients and those who were positive for the Australian antigen. This was often called the “dirty ward” at the time. Other patients were dialysed in the side ward and wards 23, 24, 26 & 27 with Kolff-Travenol twin coil dialysers. The staff was gowned and wore gloves and masks when gaining vascular access. Three patients were allocated to each machine in order to minimise any further spread of the virus.

Patients who recovered from hepatitis were trained to use home haeodialysis for fear that they may pose a risk of infection to staff and other patients if they continue to receive hospital HD. The Town Council was requested to make urgent adaptations in 6 patients' homes and the Health Committee of the Council authorised £5000 for the work. The patients were trained and transferred for home HD with little delay (Catford EF, 1984). Professor B.P. Marmion, the Professor of Bacteriology, was appointed by the Regional Hospital Board to head the Hepatitis Advisory Committee for investigating the cause of the outbreak and setting precautionary measures for the future. The staff that continued to work in the Edinburgh renal unit was well aware of the risks during the hepatitis outbreak, but their care of patients did not diminish. The charge nurse of the unit, Sister Marion Herbertson was awarded an MBE in 1971, and her comment on the award was "it is a Unit Award." (Catford EF, 1984). Until recently work on the outbreak was still going on by Professor Marmion. He believed that it was not only the Hepatitis B virus, but a combination of Hepatitis B & non-A non-B Hepatitis (i.e. Hepatitis C) virus together that gave the exceptional virulence of the outbreak (Marmion et al, 1982).

The hepatitis outbreak in Edinburgh still influences doctors' thinking about risks of infection nowadays, and was the subject of a popular novel "The Houseman's Tale" written by Colin Douglas in 1975.

Aluminium toxicity in Edinburgh (1976)

In the 1970s, there were outbreaks of encephalopathy (dementia) and bone disease (osteomalacia) in various dialysis units. This was often called "dialysis dementia". The key researchers into this were David Kerr in Newcastle and Alan Alfrey in the USA. Alfrey and colleagues associated the encephalopathy in dialysis patients with aluminium toxicity (Alfrey et al, 1976). Studies were done and a geographical variation of toxicity was found, and it was associated with aluminium in that water supply.

Water that was peaty and brown in colour was not very attractive for drinking, so was treated with alum (aluminium hydroxide) and then filtered crudely. Aluminium in the water varied enormously from one area to another. In areas with very peaty water, the aluminium level can be very high. Aluminium also came from Alucaps, (aluminium hydroxide tablets). These were used to bind phosphate in patients who were hyperphosphataemic. Alucaps, reduced

phosphate absorption from the diet. Originally it was thought that the aluminium in the Alucaps, was not absorbed into the body, but it was later found to be absorbed, increasing the plasma aluminium level. So there was a hunt for new substances to control phosphate, and calcium and magnesium were considered. Magnesium was not used since it causes diarrhoea. Calcium carbonate was chosen and used in Edinburgh in 1980s.

” I remember walking into a ward round with an article from the New England Journal of Medicine about fracturing bone disease associated with aluminium, written by a research group in Colorado.” (Dr C Swainson)
[The dialysis encephalopathy syndrome. Possible aluminium intoxication” by Alan Alfrey and colleagues, published in the New England Journal of Medicine in 1976]
“At that time one of the home HD dialysis patients was confused every time before coming into hospital, and she improved in hospital. She also had terrible fractures, but it was not due to hyperparathyroid disease. Dr Lambie thought it was an interesting article, and the patient’s condition maybe related to what was described in the article”. (Dr C Swainson)
“There was a terrible problem of encephalopathy and bone disease in the patients dialysed in Newcastle. It was called “the Newcastle bone disease”. Dialysis patients in Edinburgh also got terrible fractures. Not a week went by without at least one dialysis patient getting a fracture.” (Dr R Winney)

So the aluminium level from the water supply in her home (to the south of Edinburgh) was tested and was found to be very high. Water in the Edinburgh area was subsequently tested and the aluminium level was also found to be high. Water in Edinburgh was “medium hard”, not as hard as the water in London, but harder than the water in the Western parts of Scotland.

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Water purification

Dialysis patients are exposed to about 30,000 litres of water per year, whereas those not on dialysis are exposed to 500 to 1000 litres of water per year. Exposure

to trace elements become a significant problem to dialysis patients. Therefore there is a need to remove trace metals from the water.
Water was specially treated by reverse osmosis and using water softeners to remove aluminium. Aluminium was removed from water used for home HD using a simple technique involving ion-exchange and a modified water softener (Petrie et al, 1984).

It was recognised in Edinburgh very early on that aluminium was a major contributor to bone disease. Edinburgh was one of the first units to measure plasma aluminium routinely. It was performed in the MRU labs for many years. Research staff of the Edinburgh MRU published a number of papers regarding aluminium toxicity. Dr Robson, Dr Winney and Dr Short observed that a variable degree of anaemia was associated with aluminium toxicity. In a study in 1980, 12 patients who had high plasma aluminium developed microcytic hypochromic anaemia. 7 of the patients then went on to develop fracturing osteomalacia with 1 fatal encephalopathy. Subsequent dialysis with aluminium-free water reduced the plasma aluminium level, reversed the red cell morphology to normal, and increased the haemoglobin concentration. (Short et al, 1980).

It was shown that plasma aluminium correlated better with the presence of bone toxicity than total bone aluminium, and regular monitoring of dialysis fluid and plasma aluminium was recommended (Winney et al, 1985). Subsequent research within the renal unit has shown that low-dose aluminium hydroxide can control the plasma phosphate level without producing bone toxicity (Jenkins et al, 1989)
Nowadays the aluminium in water and patient plasma aluminium levels are still monitored, and “dialysis dementia” has become a thing of the past.

Poisoning by the mushroom Cortinarius speciosissimus

In the summer of 1979 three young adults went camping in the north. They picked some mushrooms and cooked a stew, which all three of them consumed. Two of them also ate some mushrooms raw the following morning. Two of them became significantly unwell, the third person, who only had a small amount, also felt unwell. They presented to the closest renal unit, which was the Royal Infirmary of Edinburgh. It was soon figured out that their condition was related to the mushrooms they ate. The staff got information on what the mushrooms looked

like and where they had picked them.

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PIC 1 (Psilocybe) PIC2 (Cortinarius orellaniaris)	Confusion between toxic Cortinarius species and edible or (occasionally) hallucinogenic (‘magic’) mushrooms is a regular occurence in Scandinavia, where these species are more common, but it can also occur in the UK.

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The mushrooms had orange gills and thick stipe with fibrillary striae. The mushroom was studied at the Botanical Gardens in Edinburgh and was found to be Cortinarius speciosissimus, a variant of the traditional British form. The British form is edible, but Cortinarius speciosissimus has been recognised to cause severe renal failure. It was has only been reported in 1972 in Scandinavia. Gastro-intestinal upset after 36 hours, nausea, anorexia, headache, rigors, severe burning thirst, muscle aches and oliguria are recognised symptoms and signs associated with Cortinarius speciosissimus poisoning (Short et al, 1980). One of the patients had diuresis after 8 days and had a full recovery. The other 2, who presented 10 days after consumption of the mushrooms, developed severe interstitial nephritis and did not recover renal function. They were both dialysed and were later transplanted. One of them had a kidney donated from his identical twin, and he was well without immunosuppression after the operation. The other had a kidney donated from his brother. This account was published in the Lancet in 1980, with a picture of the Cortinarius speciosissimus mushrooms, the first colour photograph ever to appear in the Lancet.