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Chronology - Blood Products/Haemostatic Agents and Hepatitis C/NANBH.

- 1965 Pool and Shannon. Production of high potency concentrates of anti-haemophilic globulin in a closed-bag system. NEJ Med. 273 page 1443

Prior to this report, the management of haemophilia rested with the administration of fresh frozen plasma and conservative measures to arrest bleeding. This article described a method of producing factor VIII enriched material using physical methods available in routine blood banking practice. The cryoprecipitate, as the material was called, was found to be comparable with the Fraction I₀ prepared by Blomback et al. (1958), which in Sweden was referred to as Factor VIII concentrate in subsequent literature.

- 1971 Newman et al. Methods for the production of clinically effective intermediate purity- and high-purity factor VIII concentrates. B J Haem. 21 page 1

This article was one of the first to describe the preparation of factor VIII concentrates of differing levels of purity from cryoprecipitate. The methods were soon applied by the private sector in the US for the commercial manufacture of factor VIII concentrates. They were quickly adopted due to their ease of use and administration.

- 1972 Kasper and Kipnis. JAMA July 31, 1972 Vol 221, No 5 page 510

This report stimulated by concerns of hepatitis after factor IX treatment (Kingdon 1970 Ann Intern Med 73: 656) reviewed the incidence of clinical hepatitis over a 10-year period in 482 haemophilia patients. In haemophilia A, a peak was observed in 1968, one year after the introduction of large donor pool concentrates as the predominant mode of therapy. The authors conclude: - "older children and adults who have had little exposure to blood products are at a high risk of developing clinical hepatitis after introduction of clotting factor concentrates. In such patients, especially those with mild haemophilia, single donor products are preferable."

- 1975 Craske et al. Lancet. An outbreak of hepatitis associated with intravenous injection of factor-VIII concentrate. August 2 1975 page 221

This public health report documents hepatitis associated with 3/4 batches of a commercial concentrate in 1974. On first use of this product, seven cases of non-B hepatitis and four of hepatitis B were seen. Two cases contracted both forms of hepatitis. Among some of the measures proposed by the authors is the recommendation that commercial concentrates should be reserved for severely affected haemophiliacs since they are more likely to be immune to hepatitis A and B. Treatment should be carried out by experienced staff who are aware of the risks of using large-pool concentrates.

- 1977 Mannucci et al. 1-deamino-8-D-arginine vasopressin: a new pharmacological approach to the management of haemophilia and von Willebrand's disease. Lancet 23 April 1977 page 869

DDAVP infusions produced an increase in factor VIII activity in patients with mild and moderate haemophilia and von Willebrand's disease. A 2-3-fold rise in factor VIII was seen during dental extraction in 4 patients with mild/moderate haemophilia. Higher DDAVP doses in patients with factor VIII levels in excess of 9% resulted in a 4-6-fold factor VIII increase. DDAVP was used for dental extractions, cholecystectomy, thoracotomy and tonsillectomy. The authors state: - "Since the average [factor VIII] rise to be expected with a single preoperative dose (0.4-0.5µg/kg) is four to six times the starting level, we suggest that

↳ Knowledge of the Danger of large pooled plasma/blood products -

basal concentrations of 8-10% are the lower limits to undertake dental extractions, whereas concentrations up to 100% can be achieved in patients with 10-20% or more, thereby allowing major surgery." "We suggest that haemostasis has been firmly established at the time of surgery by DDAVP administration, the natural concentration of factor VIII and the non-specific increase induced by surgery are likely to be sufficient to maintain haemostasis, as shown in the present series."

1977 Seeff and Hoofnagle Editorial. *Ann Intern Med* July 1977 Vol 86, No 6 page 818

Discussed the findings that suggested that *chronic* hepatitis may be common in haemophilia patients, and that this form of hepatitis could result from the consequence of treatment with blood products that could be predicted. This sequel was relevant in hepatitis B and also in the more prevalent acute non-A non-B hepatitis. Although *chronic* hepatitis expressed as persistent liver function test abnormalities in haemophilia (over 50% of cases reported) had been documented from Italy and the US since 1975, this editorial comments on the liver biopsy data presented in the same edition (Lesesne et al. 1977 *Ann Intern Med*. Vol. 86 No 6 page 703). The authors comment: - "These findings provide unequivocal evidence for the existence of *chronic* hepatitis in patients with haemophilia.

1977 Lesesne et al. Liver biopsy in hemophilia A. *Ann Intern Med*. July 1977. Vol 86 No 6 page 703

Liver biopsy was undertaken in 6 patients who had persistently abnormal liver function tests for over 6 months. Three patients had CAH and three CPH. One case with CAH had cirrhosis. The authors comment: - "It is our fear that liver disease may become a significant cause of morbidity and mortality in these patients as haemorrhagic complications are reduced with improved concentrate therapy."

1977 Hasiba et al. Chronic liver dysfunction in multitransfused hemophiliacs. *Transfusion*. Sept-Oct. 1977. Vol 17 No 5 page 490

107 HBsAg negative haemophilia patients were divided into 4 groups according to their mode of therapy and liver function parameters were assessed. Persistently abnormal transaminases were seen in 51% of patients with a large exposure to factor VIII concentrates, in 43% with a small exposure to factor VIII concentrates and in 37% exposed to prothrombin complex concentrates. In contrast abnormalities were only seen in 8% of patients treated with only cryoprecipitate. Each patient had received at least 5,000 IU factor VIII during the previous 3 years prior to the study. With respect to average transaminase values, no difference was found between the high and low exposure groups to factor VIII, but there was a significant difference between these groups and the cryoprecipitate group. The authors concluded: - "Therefore, single donor products should be the preferred mode of treatment for mild hemophiliacs who require only infrequent therapy. On the other hand, this is probably not indicated for patients requiring frequent treatment..."

1977 Mannucci et al. DDAVP in haemophilia. *Lancet* (letter) 3 December 1977. page 1171

This letter reports cases treated with DDAVP without the complication of water retention. The authors comment: - "If DDAVP treatment is restricted to patients having VIII: C 10% or higher, the basal levels of DDAVP and the non-specific increase induced by

surgery are likely to be sufficient to maintain haemostasis once this has been well established in the first 24 hrs after surgery. In patients with lower VIII: C levels, DDAVP could be adopted to reduce the amounts of anti-haemophilic globulin [factor VIII] concentrates."

- 1978 Mannucci et al. Liver biopsy in hemophilia. *Ann Intern Med.* (letter) March 1978 Vol 88 No 3 page 429

These authors report biochemical and histological data indicating that persistently elevated transaminase values most likely represent active liver disease in haemophiliacs. They recommend biopsy as a necessary and safe procedure to confirm the diagnosis and plan therapy.

- 1978 Spero et al. Asymptomatic structural liver disease in hemophilia. *NEJM.* June 22 1978 Vol 298 No 25 page 1373

14 liver biopsies were taken from 13 anti HBsAg positive patients with haemophilia and persistently abnormal liver function tests. None had any symptoms of liver disease. Histology showed CPH in 8 patients, CAH in 4 patients and early cirrhosis in 1 case. The authors state that their results suggest that there must be a large number of haemophilia patients with histological liver disease, which in some must be severe. They recommend the development of a 'clean' product (free from hepatitis B and non-A non-B hepatitis) for future treatment.

- 1978 Hruby and Schauf Transfusion-related short-incubation hepatitis in hemophilic patients. *JAMA.* September 22 1978. Vol 240 No 13 page 1355

9 episodes of short incubation hepatitis were observed in 6 haemophilic children over a 5-year period using concentrate from 2 manufacturers. In 5 patients the incubation time ranged from 4-19 days in 5 patients, while it was 8-14 days in the patient with 4 recurrent episodes of hepatitis. The findings indicate the presence of more than one non-A non-B hepatitis agents associated with factor VIII concentrate.

- 1978 Preston et al. Percutaneous liver biopsy and chronic liver disease in haemophiliacs. *Lancet* September 16 1978 page 592

The authors screened 47 haemophilia patients and found that 77% had abnormal liver function tests. Liver biopsy was under taken on 8 of these patients who were asymptomatic. A spectrum of chronic liver disease was demonstrated including CAH and cirrhosis, which bore no relation to history or biochemical findings. The authors believed that the recent development of a high incidence of chronic liver disease was probably related to factor concentrate replacement therapy. The authors comment: - "It is noteworthy that two patients with cirrhosis (1 and 7) were mildly affected haemophiliacs requiring only occasional factor VIII transfusion. Such patients may perhaps benefit from the newly developed synthetic vasopressin analogue 1-deamino-8-D-arginine vasopressin."

- 1978 Craske et al. Evidence for existence of at least two subtypes of factor-VIII-associated non-B transfusion hepatitis. *Lancet.* November 11 1978 page 1051

These authors present data indicating that there are most likely at least 2 differing strains of non-A non-B hepatitis in contaminated large donor pool concentrates.

These strains depend upon the source of the original plasma. Thus a different strain was seen in US as apposed to UK concentrate, although their incubation times were essentially similar.

- 1979 Spero et al. **The high risk of chronic liver disease in multitransfused juvenile haemophiliac patients.** *J Pediatrics*. Vol 94 No 6 page 875

Authors reported results of 87 children with haemophilia treated with plasma derivatives before the age of 21 years. 72 received factor concentrates and of these 32 (44%) had persistently abnormal liver function tests. 15 patients received cryoprecipitate or FFP only and only 1 case (7%) [that also was persistently hepatitis B Ag positive] had persistent liver function abnormalities. The majority of these 15 had mild haemophilia and thus less treatment and less total donor exposure. The authors comment their concern that 6 from 7 children under the age of 5 years treated with concentrate had abnormal liver function tests, possibly indicating that age of the patient at the time of exposure to concentrates may be an additional important factor. The authors then state their current practice: - "all patients with mild haemophilia (who require only infrequent treatment) and children under 5 years of age (regardless of their severity) who are followed in Pittsburgh are now treated only with cryoprecipitate and/or frozen plasma, each unit of which is prepared from volunteer blood donors tested negative for HbsAg by RIA. This approach is strictly adhered to unless a haemorrhage is considered to be a direct threat to the child's life, and it is felt that the episode cannot be safely treated with the less potent single donor products."

- 1979 Wyke et al. **Transmission of non-A non-B hepatitis to chimpanzees by factor IX concentrates after fatal complications in patients with chronic liver disease.** *Lancet*. March 10 1979 page 520

6 cases of non-A non-B hepatitis were described following the administration of large donor pool factor IX concentrates. From 17 patients who received the concentrate in preparation for liver biopsy on account of chronic liver disease, 4 (from the 6) developed hepatitis, which in 3 proved fatal. Transmissible infection from the concentrate was demonstrated through its passage in chimpanzees. The authors comment: - "Until blood donors can be screened for the non-A non-B hepatitis agent, it would seem wise to restrict the use of both commercial and non-commercial concentrates to life threatening situations. In particular their use in patients with chronic liver disease should be avoided as the risk of serious illness resulting appears to be increased."

- 1980 Ludlum et al. **Factor VIII and fibrinolytic response to deamino-8-D-arginine vasopressin in normal subjects and in some patients with haemophilia and von Willebrand's disease.** *B J Haem*. 45 page 499.

Six-mild/moderate haemophilia A patients were studied after DDAVP and in 4 cases an increase of factor VIII to 2 ½ basal levels were seen. No effect was seen in the other 2 patients who probably had low levels of factor VIII inhibitor. DDAVP and factor VIII kinetics were reported in this paper. The authors comment: - "DDAVP is therefore extremely useful in patients with mild haemophilia and von Willebrand's disease prior to minor surgery e.g. dental extraction, where a transient increase in factor VIII is adequate, particularly as it is more often these individuals who develop clinical hepatitis following the administration of blood products. In patients undergoing major surgery, then repeated injections of DDAVP are less useful as it may only be possible to maintain adequate factor VIII concentrations for

one day before the patient becomes refractory; the remaining 10-14 days of treatment would need to be by cryoprecipitate or factor VIII concentrate."

- 1980 McGrath et al. **Liver disease complicating severe haemophilia in childhood.** Arch Dis. Childhood 55 page 537

Very important.

Liver biopsies were performed on 5 children with severe haemophilia and persistently abnormal liver function tests. Histology confirmed CPH in 4 cases and CAH with cirrhosis in one case. The authors conclude: - "This study suggests that only brief exposure to factor VIII concentrates (13-45 batches) is necessary to produce chronic liver damage in at least 25% of haemophiliacs requiring regular treatment. As children usually receive treatment in hospital until considered suitable for treatment at home, we recommend such patients should, if possible, be treated with cryoprecipitate in preference to large pool concentrates until the significance of the chronic liver damage is better understood, or until such factor VIII concentrates have been refined to exclude viral hepatitis agents." This report is important as it describes biopsy verified chronic liver damage in children with severe haemophilia after minimal exposure to large donor pool concentrates, thus emphasising the morbidity of hepatitis in haemophilia. Additionally, the recommendation that cryoprecipitate should be used preferentially in children to limit hepatitis morbidity reflects current practice at the time.

- 1980 Sugg et al. **Clotting factors and non-A non-B hepatitis.** NEJM (letter) Vol 303 N o 16 page 943

153 patients undergoing heart surgery were studied prospectively for the incidence of post-surgical hepatitis for a period of 6 months after the procedure. Patients were assigned into 2 groups - those receiving pooled coagulation factor concentrates and those that did not. Non-A non-B hepatitis was considered present when ALT exceeded 50 IU/ml on 2 consecutive samples separated by at least one week from 14-180 days after surgery, and when markers of hepatitis A and B were absent. Non-A non-B hepatitis developed in all 8 patients (100%) treated with coagulation factor concentrates whereas only 4/145 (3%) of the untreated patients had signs of hepatitis. These results emphasise the high risk of transmission of non-A non-B hepatitis from un-sterilized pooled plasma derivatives.

- 1980 Hasiba et al. **Liver dysfunction in Pennsylvania's Multitransfused Hemophiliacs.** Dig Dis Sci. October 1980. Vol 25 No 10 page 776

The authors report a study evaluating the effects on the liver of repeated exposure to plasma derivatives in a large group of closely monitored haemophilia patients. 558 patients with coagulation disorders who had been treated with plasma derivatives were studied at 8 major centres during the period 1973-1978. The patients were divided into concentrate group (435 patients) and cryoprecipitate group (79 patients). Persistently abnormal liver function tests were found in 31% of the concentrate group and in 2% of the cryoprecipitate group, the difference being significant ($p < 0.05$) particularly at the two lowest dosage ranges studied. The authors stated that the lesser degree of liver function abnormalities in the cryoprecipitate treated group persists in those receiving up to 50,000 units (approximately 600 bags) over 6 years but seems to disappear in patients receiving more.

- 1981 Norkrans et al. Acute hepatitis Non-A non-B following administration of Factor VIII concentrates. *Vox Sang.* 41 page 129

The authors report a retrospective study on 20 patients with mild haemophilia A or von Willebrand's disease. Nine episodes of non-A non-B hepatitis occurred in 8/20 (40%) who had been treated for the first time with commercial factor VIII concentrate (>2000 paid donors). This compared with an incidence of 8% in the patients after treatment with a Scandinavian factor VIII concentrate prepared from a smaller donor pool (100-250 voluntary donors). Chronic liver disease occurred in 3 of the infected patients. This paper emphasises the higher risk of developing hepatitis from large donor pool concentrates.

- 1981 Leading article on Post-transfusion hepatitis. *BMJ* 4 July 1981 Vol 283 No 6283 page 1

This important leader in a general medical interest journal of wide distribution clearly describes the problems of hepatitis in haemophilia, as they were perceived at the time. The author starts by stating that post-transfusion hepatitis remains the major complication of modern haemophilia management, and emphasises the mortality and morbidity of hepatitis in this patient group. The stress is put on non-A non-B hepatitis as the commonest form of hepatitis in haemophilia, and comment on the greater infectivity of hepatitis following transfusion of paid donor blood rather than volunteer blood is made. Major discussion is made over the controversy in the size of donor pools to prepare plasma derivatives, and reference is made to Seeff et al recommendations and of those by Craske et al in 1975. Of note is the report by Stirling et al on the follow up data over 5 years in haemophilia patients receiving concentrate or cryoprecipitate. There was no association between the use of cryoprecipitate and liver function impairment, while this was clearly the case with patients receiving concentrate.

- 1981 Stirling et al. Liver function in Edinburgh haemophiliacs: a five-year follow-up. *J Clin Path.* 34 page 17

Data was collected from 38 haemophilia patients, 7 of whom had been treated almost exclusively with factor VIII concentrate while the remaining 31 had received predominantly cryoprecipitate. Deterioration in liver function tests over a five-year period was seen only in patients on home treatment using large amounts of factor VIII concentrate. There was no association between cryoprecipitate usage and derangement of liver function. No liver biopsies were performed on the clinical material. The authors comment: - "Meanwhile there does not appear to be sufficient evidence of any serious deterioration in liver function from NHS concentrate to limit its current use in patients on home treatment, for whom the convenience of the product is all important. It would seem reasonable, however, that patients in hospital should whenever possible receive non-pooled cryoprecipitate instead." Accepted for publication May 1980.

- 1981 Crawford and Mitchell. Post-transfusion hepatitis. *Lancet* (letter). August 8 1981 page 312

These authors, both distinguished in the field of blood transfusion, recommended that the use of large donor-pool coagulation products should be kept to a minimum until suitable markers against non-A non-B hepatitis were made available. To this end, they introduced small pool dried cryoprecipitate to the UK.

- 1981 Gabra et al. Post-transfusion hepatitis. *BMJ (letter)* 8 August 1981 Vol 283 page 439

This letter responds to the leading article on post-transfusion hepatitis in 4 July copy of the *BMJ*. With respect to the preparation of safe blood products, the authors refer to the national policy of Switzerland where treatment of haemophilia is based upon small pool freeze dried cryoprecipitate, while large donor pool concentrates are reserved for severely affected patients and those with factor VIII inhibitors. The authors refer to the current product they have produced for Scotland since 1979. This product is a cryoprecipitate from one litre of plasma (average yield 400 IU factor VIII activity) obtained by small pool preparation using 5-30 donations of plasma. They report that this product was current treatment at the large Glasgow Haemophilia Centre and that the product was under assessment in 2 separate clinical trials in Scotland. The authors conclude: - "We believe that until a reliable test for the markers of non-A non-B hepatitis becomes available small-pool products such as cryoprecipitate should be considered whenever possible for all haemophiliacs, particularly paediatric patients with limited exposure to blood products, and for patients with mild and moderate disease expected to have infrequent therapy."

- 1981 Bamber et al. Short incubation non-A non-B hepatitis transmitted by factor VIII concentrates in patients with congenital coagulation disorders. *Gut* 22 page 854

The authors reported 10 cases of non-A non-B hepatitis developed 1-4 weeks after they had received factor VIII concentrate or cryoprecipitate. It is of interest to study the previous infusion history as summarised in Table 1. Five patients (5/5) received factor VIII concentrate for the first time although they all had previously received various amounts of cryoprecipitate at different times. The other 5 patients who developed non-A non-B hepatitis were all well established on regular cryoprecipitate treatment at 1-4 weekly intervals. All 10 patients had an incubation time of 1-4 weeks from the last infusion of plasma derivative, demonstrating the previously described short incubation agent. These data demonstrate that there was a 100% incidence of non-A non-B hepatitis in patients, previously treated exclusively with single donor pool materials, on first exposure to large donor pool products. The patients who had continued to receive cryoprecipitate yet developed hepatitis indicated that the infective agent was also present in single donor materials but clearly the incidence of hepatitis was far lower with these products. All the infected patients in this series developed chronic hepatitis.

- 1982 Cederbaum et al. Abnormal serum transaminase levels in patients with hemophilia A. *Arch Intern Med.* March 1982 Vol 142 page 481

A co-operative study of 1332 haemophilia patients who underwent 3 serial liver function tests during a six-month period demonstrated that 72% of patients had one elevated transaminase value while 21.1% and 23.6% had persistently elevated SGOT and SGPT values on the 3 serial measurements. Patients untreated during one year showed fewer abnormalities than those treated. Patients who received less than 50 IU/kg per 6 months had fewer abnormalities if the material given was cryoprecipitate than if they had received concentrate. However, these groups were not strictly comparable as the cryoprecipitate group contained a greater proportion of mildly affected haemophilia patients than the concentrate group, and prior total exposure was less.

1983 Product Safety. Distributed on 24 June 1983

General recommendations made at meeting on 13 May 1983

For mildly affected patients with haemophilia A and von Willebrand's disease... This... recommends the consideration of the use of DDAVP instead of large pool

1983 Warrier et al. **DDAVP: a useful alternative to blood components in moderate haemophilia A and von Willebrand's disease.** J Pediatrics Vol 102 No 2 page 228

DDAVP intravenously (0.2 µg/kg) and intranasally (2-4 µg/kg) was studied in 3 normal individuals, 31 subjects with von Willebrand's disease and 7 cases of mild or moderate haemophilia A. All cases except one hemophilic increased their factor VIII activity by more than 200%. In the 4 patients with mild/moderate haemophilia (VIII: C 3-12 iu/dl) factor VIII levels increased by 2 and a half to 6 fold in all cases. Eight patients (7 with vWD and 1 with haemophilia) underwent surgery with DDAVP cover instead of cryoprecipitate. Surgery included 3 tonsillectomies, 3 dental extractions, 1 minor oral surgery and one nasal polypectomy. The latter case with moderate haemophilia experienced a VIII: C rise from 2 to 13 iu/dl. DDAVP was also given successfully in 2 haemophilia patients for the treatment of 3 episodes of acute haemarthrosis and one soft tissue haemorrhage. No adverse effects were observed in the 41 subjects studied. The authors state: - "An alarming number of persons who developed viral hepatitis, especially non-A non-B hepatitis develop a chronic or chronic-active form of hepatitis. Thus an alternative to the use of blood products seems to have distinct merit. For at least some individuals with hereditary bleeding disorders namely those with mild or moderate haemophilia A and those with von Willebrand's disease, the vasopressin analogue DDAVP appears to be a safe and reasonably effective alternative to treatment with blood products." "In individuals with haemophilia A, this selection (for clinical benefit with DDAVP) can be made on the basis of the patient's usual factor VIII level. Those with factor VIII activity 5 to 20 iu/dl (5-20%) would seem ideal candidates for treatment with DDAVP whenever a threefold increase in factor VIII activity of several hours duration would be sufficient treatment." This report is important since it reveals that DDAVP can be given safely to mild/moderate patients with haemophilia undergoing surgical procedures.

1983 Internal correspondence from DHSS – Diana Walford dated 6 June 1983. Under the general heading "Possible Implications of AIDS for Plasma Supply and Manufacture at BPL"

"There are increasing indications that the AIDS may be transmitted by blood and blood products. Because of the number of donations to which they are exposed, haemophiliacs receiving large pool factor VIII concentrates (such as that manufactured at BPL) might be at greater risk than those receiving single donor cryoprecipitate or small pool products.]

At a recent Council of Europe meeting (16-19 May 1983) a draft resolution was accepted which recommends that the use of coagulation factors prepared from large plasma pools should be avoided except where such a product is specifically indicated for medical reasons. The implication in the resolution is that there should be a greater use of single donor or small pool products."

This information is important not only in the context of AIDS prevention but, in view of the lengthy and detailed reports in the literature, is also relevant with regard to non-A non-B hepatitis in haemophilia.]

1983 UKHCDO Recommendations on Blood Product Safety. Distributed on 24 June 1983

General recommendations made at meeting on 13 May 1983: -

1. For mildly affected patients with haemophilia A and von Willebrand's disease.... This item recommends the consideration of the use of DDAVP instead of large pool

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concentrates in these patient groups. From the correspondence from the DHSS, it is clear that the NHS freeze dried concentrate from BPL was classified as a large pool concentrate - see also reports in the literature e.g. Fletcher 1983.

- 2. For the treatment of children (presumably with all forms of haemophilia and all types of severity - as recommended in the literature) and mildly affected patients or patients unexposed to imported concentrates..... This item specifies that NHS materials should be used preferentially, and cites the two types of products available through the NHS. For mildly affected patients, combining items 1 and 2 eliminates the prescription of large donor pool products of commercial AND NHS origin, and leaves the treatment option of cryoprecipitate that is consistent with all recommendations in the medical literature for these categories of patients.

Collins Case

WMAJ 83.

1983 US National Hemophilia Foundation Recommendation. Cited in Blood Policy and Technology 1985 Op. Cit. page 101

In October 1983, the US National Haemophilia Foundation specifically recommended that cryoprecipitate be used to treat babies and infants aged under 4 years old, new patients and mild cases. Although this recommendation was issued specifically to reduce the incidence of transfusion transmitted AIDS, the recommendation applies equally well to non-A non-B hepatitis in the same patient categories.

Collins

1983 Collins et al. Prospective study of post-transfusion hepatitis after cardiac surgery in a British centre. BMJ 12 November 1983 Vol 287 page 1422

The authors report a series of 248 patients undergoing heart surgery who received blood and/or plasma derivatives. This prospective study determined post-transfusion hepatitis in the recipients of the blood/plasma derivatives. The incidence of post-transfusion short incubation non-A non-B hepatitis was considered to be 2.4%, although the frequency of blood sampling raises some doubt as to the validity of the diagnosis. Although the mean plasma donor units transfused to each recipient was 6.28, an estimate of the incidence of infection in relation to the transfusion of 1 donor unit was not made. With the exception of 2 of these cases, normal liver function was demonstrated in this infected group after 1 and 6 months, which may further question the validity of this data and cast doubt of the methods used in the establishment of the diagnosis of hepatitis. Chronic liver disease after post-transfusion non-A non-B hepatitis was thought to be 0.4% but still related to the mean of 6.28 donor units of transfused material. This report is of interest in that the study was performed before the DOH programme of donor self exclusion was implemented, and thus these figures are probably greater than figures relating to treatments given from 1983 onwards (as the report was accepted for publication in August 1983). The results do not give information on the prevalence of non-A non-B hepatitis in the donor population nor the hepatitis risk per unit of single donor blood/plasma derivative. It is also of interest that a similar study from the Netherlands stated that blood tests taken within 2 weeks of surgery were not reliable indices of NANBH and thus much of the acute NANBH described by the authors must be questioned. As all the patients in this litigation have shown evidence of chronic NANBH with persistently raised transaminase values well beyond 6 months after infection, it would seem appropriate to use incidence figures of NANBH from the literature which relate exclusively to chronic liver disorders consequent to NANBH.

Knowledge of the Danger of large donor plasma/blood products