Professor Steer comments:

I am grateful for the comments by Drs Seidman and Mashiach. However they seem to have misread my review because they claim that I stated that up to three digital vaginal examinations have no effect on provoking labour. In fact I suggested that 'careful cervical assessment should be made on all women' and that 'up to three (examinations) when they (the membranes) are ruptured'. Nowhere do I state that the examination should be digital, and I agree with Drs Seidman and Mashiach that 'virtually all the information necessary can be obtained from a sterile speculum examination'. I also agree that this need only be performed once if a decision is made for conservative management. However, if subsequently there are signs of active labour supervening, then usually the only way of establishing whether this is really the case is to repeat the examination. Usually a speculum examination is sufficient, but very occasionally if the mother is uncooperative a digital examination may be necessary as a last resort.

In relation to the risk of digital examination, I am grateful for the references supplied; it should be noted however that of the four sources given, two appeared after I prepared my manuscript and a third remains unpublished.

Rh haemolytic hepatitis

SIR,—In his recent article on Rh haemolytic disease Professor Whittle states that extra-medullary erythropoiesis secondary to fetal anaemia may obtrude other liver activities, leading to reduced albumin production and hydrops fetalis.¹ However, clinical, biochemical, and histological studies made in Birmingham,² Bristol,³ and San Francisco* between 1960–7 shows this not to be so. Indeed, some hydropic infants that I studied at necropsy had no hepatic erythropoiesis. Instead, the explanation for the liver failure was in widespread liver cell damage to be found in 10–20% of the most severely affected Rh infants. Characteristically, such infants demonstrated obstructive jaundice, marked hepatosplenomegaly, and cord blood haemoglobin concentrations below 100 g/l. Half the infants, with a mean total cord serum protein concentration of 31 g/l and a mean serum albumin of 16 g/l, exhibited hydrops fetalis. Prenatal growth retardation, haemorrhagic disease of the newborn, and neonatal hypoglycaemia were common complications, probably also secondary to the liver damage.

During this eight year period I observed only three Rh infants with signs of kernicterus. All had exhibited cholestasis. None had had 'dangerous' concentrations of serum unconjugated bilirubin. It seems likely in retrospect that these infants had had low serum albumin binding capacities.

Microscopically, the liver architecture was grossly disorganised and the hepatic cells, often multinucleated, were loaded with haemosiderin. Reticulum and collagen fibres were markedly increased, even occasionally to the point of early cirrhosis.

My studies led me to speculate that the liver damage, which I termed 'Rh haemolytic hepatitis' was due to the sequestration and sludging of agglutinated red cells in the

hepatic sinusoids leading to secondary hepatic hypoxia and also to haemosiderosis. I further suggested that this was only likely to occur to any significant extent after haemolytic 'overload' had led to a splenic failure to deal adequately with the damaged circulating red cells. I still think this is likely to be the correct explanation.

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- 1 Whittle MJ. Rhesus haemolytic disease. *Arch Dis Child* 1992;67:65–68.
- 2 Dunn PM. Obstructive jaundice and haemolytic disease of the newborn. *Arch Dis Child* 1963; 38:54–61.
- 3 Dunn PM. Obstructive jaundice, liver damage and Rh haemolytic disease of the newborn. *Bulletin of the Jewish Hospital (New York)* 1965;10:92–124.

*(A) Dunn PM. Cholestasis and erythroblastosis fetalis. Paper presented to University of California School of Medicine, San Francisco, 29 June 1967. Manuscript unpublished but available on request.

(B) Dunn PM. The significance of liver damage in severe erythroblastosis fetalis. Paper presented to the Neonatal Society, London, 2 November 1967. Manuscript unpublished but available on request.

Professor Whittle comments:

Professor Dunn seems to suggest that extra-medullary erythropoiesis in the liver is unlikely to be the cause of impaired liver function in the baby affected by severe Rh disease and suggests a condition of Rh hepatitis as an alternative. Indeed he states that some of the cases of hydrops that he described showed no evidence of hepatic erythropoiesis, a most surprising observation. The references he uses are all his own, but Wigglesworth and I suspect, most pathologists seem to have less doubt that the liver and spleen are largely replaced by erythropoietic activity in severe Rh disease.¹ Nevertheless it may well be true that such activity and the general tissue hypoxia which exists in the very anaemic baby may produce hepatic damage, but probably as a very late stage event. Hydrops, on the other hand, will usually appear once the fetal packed cell volume has fallen to about 0.15 and some time before eventual death. It should be further noted that whereas the changes described by Professor Dunn would be likely to be irreversible, hydrops will resolve once the baby has received appropriate transfusions and presumably hepatic erythropoiesis has become suppressed and normal activity recommenced.

- 1 Wigglesworth JS. The liver and biology system. *Perinatal pathology*. Philadelphia: W B Saunders, 1984:317.

Low dose intraventricular fibrinolytic treatment to prevent posthaemorrhagic hydrocephalus

SIR,—The report of Whitelaw *et al* on the use of intraventricular streptokinase is of interest.¹ However, I am not convinced that their very good clinical outcomes were due to fibrinolytic enhancement. Streptokinase acts by combining with plasminogen with the resultant strepto-

kinase-plasminogen complex being the plasminogen activator. It is well established that human newborns have moderate to severe hypoplasminogenemia. This limits the amount of plasmin that could be generated. Also, the in vitro fibrin plate method that the authors used employed human fibrinogen. This reagent contains plasminogen unless the laboratory specifies plasminogen-free fibrinogen. Thus, the zones of lysis that the authors noted could be due to streptokinase in the cerebrospinal fluid combining with plasminogen in the fibrin plate and not being indicative of true fibrinolytic activity in the cerebrospinal fluid.

The authors should clarify if the human fibrinogen reagent contained plasminogen or not, and, if it did what other evidence do they have that indeed they induced a lytic condition.

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- 1 Whitelaw A, Rivers RPA, Creighton L, Gaffney P. Low dose intraventricular fibrinolytic treatment to prevent posthaemorrhagic hydrocephalus. *Arch Dis Child* 1992;67:12–4.

Dr Whitelaw and coauthors comment:

We appreciate Professor Corrigan's interest in our paper. He questions whether we have evidence of a fibrinolytic state in the cerebrospinal fluid (CSF) during intraventricular streptokinase treatment. He is quite right in pointing out that laboratory grade fibrinogen contains small amounts of plasminogen and therefore streptokinase could have produced lysis on the fibrin plate without there necessarily being plasminogen already present in the CSF. However, we have been able to demonstrate the presence of plasminogen in CSF after intraventricular haemorrhage using an immunodiffusion method and this will be published in a future paper. The plasminogen then becomes undetectable in CSF during streptokinase treatment because it becomes incorporated in the active streptokinase-plasminogen complex. Further evidence of plasminogen activation is provided by the finding of high concentrations of fibrin degradation products in the CSF after intraventricular haemorrhage,¹ and a pilot study we have done also shows that the concentrations of fibrin degradation products rise during intraventricular streptokinase treatment. It is significant that the CSF taken before streptokinase treatment produced lysis on the fibrin plate. Finally, the intraventricular bleeding occurring during streptokinase infusion in one baby is consistent with a fibrinolytic state within the cerebral ventricle.

Thus we are accumulating evidence (which will be published in full) that there is considerable endogenous fibrinolysis in the CSF following intraventricular haemorrhage and that it is possible to augment this fibrinolysis by intraventricular streptokinase.

- 1 Whitelaw A, Creighton L, Gaffney P. Fibrinolytic activity in cerebrospinal fluid after intraventricular haemorrhage. *Arch Dis Child* 1991;66: 808–9.