ANALYSIS OF AMNIOTIC FLUID IN THE MANAGEMENT OF THE RHESUS-SENSITIZED PREGNANCY*

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In the management of the Rh-sensitized pregnancy there is now general agreement that early induction of labour favourably influences the course of selected cases. In severe haemolytic disease of the newborn, early induction may mean the difference between a premature infant salvable by exchange transfusion and a stillborn hydropic one at term. In making the weighty decision to induce premature labour, and in balancing the risks of prematurity against those of erythroblastosis, the degree of involvement of the infant under review is acutely felt. Complete information regarding both parents' blood groups and Rh genotypes, past obstetrical history, and antibody titres in previous pregnancies, together with regular antibody levels throughout the current gestation, are vital before an assessment of any sort can be made. In the hands of such workers as Kelsall and Tovey and their colleagues,[1, 2] using the indirect antiglobulin technique, good correlations have been achieved between antibody titre and degree of foetal involvement.

Nevertheless, predictions based on antibody study are subject to well-recognized weaknesses. Even in the hands of those most enthusiastic about antibody predictions, nothing like the same degree of accuracy as in first-affected babies is achieved in second or subsequently affected

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babies, where surprise results are common, with severe affection following low antibody levels during pregnancy and *vice versa*. The difficulty is particularly marked when the father is heterozygous. Furthermore, many laboratories have not been able to reproduce the good correlation between antibody levels in pregnancy and the degree of affection in the baby as achieved by the workers mentioned. It is difficult to obtain a close standardization between the end-point of antibody titres from different laboratories, so that a comparison between results is of little value.

But the major weakness from our point of view is the frequency with which one is confronted with inadequate information in a given sensitized pregnancy. Often, antibody estimations or even blood grouping have never been done in previous pregnancies or the first antibody estimation is performed only after the 30th week. The father's genotype is more often than not unknown.

Under these circumstances, a direct assessment of the foetus itself is sorely needed, and such a direct method is to be found in the examination of liquor amnii for its content of bile pigments. We have been using this technique in Bulawayo over the past 18 months and, though the number of cases is small, we have been impressed by its usefulness and feel that we can add a little weight to the growing mass of evidence that suggests that amniocentesis should be an essential investigation.

Over 110 years ago Bevis[3] first observed that the degree of bile pigmentation of the amniotic fluid of foetuses affected by haemolytic disease had prognostic significance. Walker and Jennison[4] confirmed this and found that spectrophotometric curves of fresh specimens correctly predicted erythroblastosis foetalis in 95% of their cases. Naked-eye assessment of colour or use of the icteric index are dangerous oversimplifications, for haemoglobin in dilution imparts a jaundiced tinge that has no prognostic value. Direct spectrophotometric measurement of bilirubin, though applicable to serum, is unsuitable for liquor because of interference by haem pigments and opalescence due to vernix caseosa. For empirical purposes, however, an assessment of the bilirubin is possible from the spectral absorption curve of liquor, since bilirubin produces a peak or deviation of 450 mμ, while in unaffected babies absorption is approximately linear from 365 to 550 mμ. Liley has investigated the height of the peak at 450 mμ in 101 sensitized cases and has evolved a scheme for the prediction of the degree of foetal involvement from the bilirubin peak and the gestational period. We have used his nomogram in our predictions and find the method reliable. From the position of the plot, and the slope of a line from this to any subsequent plot, a practical guide to the management of a case has been drawn up.

Liquor amnii is obtained from the 30th to the 35th week by transabdominal puncture, by means of a medium-sized lumbar-puncture needle. The abdomen is usually entered on the side opposite to the baby's back and just below the umbilicus when the vertex is presenting. A pool of liquor amnii is present between the infant's limbs and no difficulty is usually found in obtaining the fluid. In breech presentations the puncture is made a little higher. Those interested in a full description of the technique of amniocentesis and spectrophotometric study of the liquor are referred to the comprehensive papers of Liley[5, 6] and Walker and Jennison.[4]

Dangers and Limitations

In a recent series of 253 abdominal amniocenteses,[11] one foetal death is described, caused by puncture of a large placental vessel. This is the only accident directly attributable to the puncture that I have been able to find in well over 1,000 amniocenteses.[4, 5, 7-9] In 200 performed for various reasons. Liley reported 2 cases of amnionitis with resultant foetal loss. Moncrieff's strictures[10] about the possible danger of a lethal rise in maternal antibody after amniocentesis, due to the passage of foetal cells into the maternal circulation, were based on a single case, and yet this statement did much to throw the procedure into disrepute. Kelsall, however, has informed me of 2 similar cases where, 7 - 10 days after tapping, maternal antibodies were found to have risen from 1 in 128 to 1 in over 1,000. Of course there is no way of knowing whether this rise in titre would not have occurred if the tapping had not been done. Contamination of liquor by maternal or foetal blood is found from time to time, but does not seem to cause ill-effects. Foetal serum, however, causes a rise in the peak on 450 mμ and invalidates the results.

As in any other surgical procedure, there are thus very slight but definite risks present. These are outweighed by the potential importance of the information to be gained.

An undoubted drawback to the method is the gradual fall of the bilirubin levels in the amniotic fluid after the 35th week. There will therefore, though rarely, be cases with marked rise in antibody levels during the last weeks of pregnancy in which the amniotic fluid will not show any abnormal bilirubin peak.

The risk of placental puncture, and consequent foetal haemorrhage and the possible but as yet unproved danger of a lethal antibody rise, might be obviated by accurate localization of the placenta before selecting a site for amniocentesis. This can be achieved by careful clinical examination, auscultation for a funic souffle and, if necessary, radiography.

Indications

There can be no doubt that examination of the amniotic fluid must form an indispensable part of the investigation in certain cases, even in a first-class centre with centralized laboratory facilities. Where the mother has already had one affected baby and the father is heterozygous, antibodies will seldom be of much help, even in the best hands, for there is rarely a sudden drop to show that the infant is Rh-negative, nor a dramatic rise to indicate a sensitized one.

On the other hand, when the father is homozygous and it is therefore certain that the infant will be erythroblastotic, amniocentesis will in most cases merely confirm the prediction based on antibodies and on the previous history. Where the infant is severely affected and too immature for induction, this information is a reassurance to the mother and the practitioner that everything possible has been done. If the infant is salvable, accurate guidance to management can be given; and surprise results are so frequent in second or later sensitized pregnancies that amniocentesis is always worth while.

The study of the amniotic fluid will prove of most use in the incompletely investigated pregnancy and where antibody results are unreliable.

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