was supported by psychiatric opinion, and she was given an anterior-chamber implant. The visual result was good, with an acuity of 6/6 and full binocular vision. Shortly after the operation she was released from the mental hospital and is apparently leading a normal domestic life.

Case 4

A Polish boy arrived in the United Kingdom in 1939 as a 1-year-old refugee. At the age of 12 he was hit in the right eye by a piece of wood, which produced traumatic aphakia. He developed a well-marked divergent squint, which was later considerably reduced by appropriate surgery. He became very depressed about his near-unioocular condition, and could not settle down in this country. He therefore applied to emigrate to Canada. In the meantime, at the age of 20, he obtained my opinion on the possibility of restoring useful sight to this eye with an anterior-chamber implant. I thought that this was possible, but at that moment he was told that he had been accepted by the Canadian Emigration Authorities and could leave in two months' time. I told him that it would not be possible to do this operation and see him through the convalescent period within this time, and that he had to choose between staying in this country for a year or so and having this operation done, or forgetting about it and emigrating to Canada. He decided that his eye was more important than emigration, and implant surgery was carried out. He now sees 6/6 and is very pleased. He has got a better job in this country, and is no longer so keen on emigrating.

Case 5

In 1944 two nurses were listening to the 9 o'clock news in the sitting-room of the nurses' home attached to a south coast hospital when one of the last shells fired by the Germans across the Channel scored a direct hit. One nurse was killed outright and the other received a perforating wound of the left eye. This iris prolapse was abscised and the wound healed. A traumatic cataract developed over the next year or so and eventually she was given a pension of 15s. a week by way of compensation. She subsequently married, gave up nursing, and had two children, but she found life as a one-eyed person rather trying, and her children did not hesitate to tease her, sometimes unkindly, about her disability.

When first seen 13 years later, at the age of 44, she had an inferior iris coloboma with a traumatic cataract. The cataract was extracted intracapsularly with some difficulty, because the lens capsule had become adherent to the limbal scar below. Three months later an anterior-chamber implant was inserted. The patient now sees 6/6 with a small correction, and has full binocular vision. In this case the patient was always psychologically well adjusted and no great change in her morale is yet noticeable; possibly her long contact with the medical profession has made her view the achievements of surgery with a certain scepticism, and perhaps she wonders if this happy result will last.

Discussion

The above examples suggest that it is possible to restore useful visual function to cases of unioocular aphakia many years after the original injury and at the same time to effect a notable improvement in the psychological well-being of the patients. It would clearly be better if such injuries were corrected in this way before amblyopia, squint, and psychological damage had appeared. The purpose of the operation, and the fact that it is proposed to insert a foreign body into their eyes, must, of course, be made clear to the patients, but in my experience the large majority of those with unioocular aphakia are very conscious of their disability and are not deterred by references to the experimental nature of this work. They want an improvement in their vision as soon as it can be arranged, and are not concerned at the possibility of

complications, either immediate or delayed. Two of the patients in this series were so unhappy with their almost useless eyes that they requested that these be removed should they be considered unsuitable for implant surgery.

Summary

The rationale of the treatment of unioocular aphakia by means of anterior-chamber implants is described.

The first 100 cases treated at the Southend General Hospital are reviewed; the immediate results are regarded as satisfactory.

Another 5 to 10 years must elapse before the long-term results can be accurately assessed.

In the meantime, this operation can be offered with reasonable confidence to persons with unioocular aphakia who are worried by their disability and are anxious for treatment.

This piece of clinical research has entailed extra work for a busy department, and I am grateful to my colleagues, especially Dr. R. A. Owen, ophthalmic registrar, Dr. J. Alfred Lee, senior Anaesthetist to the Group, and to Sisters Cockerill and Gugarel, for their valuable assistance. The Southend-on-Sea Hospital Management Committee has been very understanding and helpful about the additional expenditure on this work, and as a result the extra funds have been made available without our having had to apply for or to obtain a grant in aid of this research. My thanks are also due to Rayner Ltd. for their close and helpful collaboration.

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ANTE-PARTUM MECONIUM STAINING OF THE LIQUOR AMNII

BY

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The discovery of meconium staining in the liquor amnii before the onset of labour raises a problem in management, and this paper is an account of the results obtained when an expectant course is adopted in the large majority of cases.

Meconium staining of the liquor amnii in labour has long been regarded by obstetricians as an adverse sign so far as the foetus is concerned; indeed, meconium appearing in liquor which had been clear earlier in labour is perhaps the most absolute sign of foetal distress. Lister and Buchanan (1957), in an investigation of the signs of foetal distress, found that of all single factors the passage of meconium gave the worst prognosis for the foetus. In their series the babies in 50% of the cases in which meconium was passed showed some signs of asphyxia at birth. For the purposes of their investigation they regarded a baby as asphyxiated if it did not cry within one minute of birth. The findings of Lister and Buchanan are in agreement with those of FitzGerald and McFarlane (1955).

Another view is that of Desmond *et al.* (1957), who considered meconium to be a marker for hypoxia and evidence that the foetus may become dangerously hypoxic during the remainder of the birth. In their series meconium was passed in 10.9% of cases: in these cases 77.2% of the babies had no difficulty in breathing at birth and in 22.8% there was difficulty of varying degree. This latter figure represents a threefold increase over a control series of cases. In conclusion, these authors stated that meconium staining of the liquor amnii does not imply that the foetus is in extreme distress but rather is close to its tolerance limits. Burger *et al.* (1956) studied the effect on the foetus of the intra-partum passage of meconium in 172 cases. In 79 of them no cause for the passage of meconium was found, and they thought that the passage of meconium by itself was not significant other than that it was an alarm signal.

Ante-partum meconium staining is discussed in the Blair-Bell Memorial Lecture given by J. Walker in 1954 and by Macafee and Bancroft-Livingstone (1958). Walker stated that meconium staining in the liquor was due to a deficient oxygen supply to the foetus, and that the saturation of oxygen in the umbilical vein was at or below the critical level of 30%. Death from anoxia is preceded by meconium staining of the liquor for a variable period of time. On these grounds Walker urged the performance of caesarean section when heavy meconium staining of the liquor is encountered at artificial rupture of the membranes, and this was particularly indicated in primigravidae over the age of 30, since in these cases the incidence of prolonged labour is relatively high. Walker further stated that observation of the foetal heart was not a good guide, as frequently it stops suddenly without any period of slowing or irregularity. Macafee and Bancroft-Livingstone disagree with Walker's views and believe that the appearance of meconium is a danger which has been over-emphasized.

Analysis of Cases

Artificial rupture of the membranes as a means of inducing labour is carried out in about 15 to 20% of cases admitted to Bellshill Maternity Hospital, and I have analysed a series of cases covering the three-year period 1955-57. In this period 2,054 surgical inductions of labour were performed, and in 125 of these the liquor was found to be meconium-stained—an incidence of just over 1 in 16 cases. There were 51 primigravidae and 68 multiparae in the series.

When meconium staining of the liquor is encountered the management is as follows. Any change in the foetal heart rate as a result of the induction is noted. Note is also taken of factors such as the patient's age, parity, and obstetric history. In some cases a decision to perform immediate caesarean section may be taken where there has been a significant alteration in the foetal heart rate or where other factors such as a bad obstetric history or severe toxæmia of pregnancy are present. In most cases, however, an expectant policy is pursued. The foetal heart rate is charted at 15-minute intervals for a few hours after the surgical induction; if, however, there is no alteration in the heart rate then charting is not continued to the interruption of the patient's sleep but is restarted at the onset of labour and continued until delivery.

In this series there were nine stillbirths and one neonatal death. This represents a perinatal mortality

rate of 8%. The corrected rate is 2.4%, as in seven of the cases the foetus was abnormal—five cases of anencephaly, one case of hydrocephaly, and one case of hydrps foetalis. If another case in the series in which the baby was alive at the end of a month but had a severe degree of spina bifida is considered then the incidence of an abnormal foetus in association with ante-partum meconium staining of the liquor is the high figure of 6.4%.

With regard to the remaining stillbirths, one occurred in a primigravida who developed a severe mixed accidental haemorrhage. The second case was that of a gravida-2 aged 32 in whom labour was induced at the 41st week of pregnancy on account of prolongation of pregnancy. The latent interval before the beginning of labour was 20 hours 40 minutes and labour lasted four hours five minutes. The foetal heart was said to have disappeared suddenly in early labour, but on investigating this case it appeared that there was a vital gap of one hour in which the foetal heart was not recorded, and it may be that this stillbirth would have been prevented had the failure to maintain the foetal heart chart not occurred. Nevertheless, it cannot be said that in this case the foetal heart did not stop suddenly; but, even assuming that it did so, it still represents an incidence of less than 1%.

The one neonatal death that occurred was said to be due to asphyxia, and at the post-mortem examination plugs of meconium were found in the bronchi. The mother was a gravida-2 aged 22 in whom labour was induced a few days before term on account of rhesus iso-immunization. The latent interval before the onset of labour was 18½ hours and labour lasted three hours. The baby, which weighed 9 lb. (4.1 kg.), was delivered spontaneously, but was very cyanosed at birth and remained so in spite of resuscitative measures. It died after 6½ hours. Study of the foetal heart chart in this case revealed that, although the foetal heart rate remained regular, there was an increase in rate from 120 to 160 beats a minute.

The number of caesarean sections performed in these 125 cases was 20, which is a caesarean section rate of 16% as against the hospital rate of 7.9%. In 13 of these cases the patients were primigravidae, while in a further three the only previous pregnancies had been abortions. Eleven of the women were not in labour. In the nine cases in labour the indication for caesarean section was foetal distress as evidenced by slowing or alteration of the foetal heart rate; foetal distress was also the indication for six of the cases not in labour. Severe pre-eclamptic toxæmia was the main indication in four of the other cases not in labour, while accidental haemorrhage was the indication in the remaining case. There was no foetal mortality among the cases delivered by caesarean section.

Eighteen cases in the series were delivered by forceps, representing a rate of 14.4% as against the hospital rate of 8.3%, so that again the rate for the series is almost double the hospital rate. None of the 18 babies was lost. In nine cases forceps were used solely on account of foetal distress, and in eight there was second-stage delay, due usually to a deep transverse arrest or to a persistent occipito-posterior position of the vertex. The remaining case was a patient in whom mitral valvotomy had been performed during pregnancy. Eleven of the cases were primigravidae and seven were multiparae.

Operative delivery was performed in a further six cases. Four were assisted breech deliveries, one was a case of twin pregnancy in which both babies required manual breech delivery, and the remaining case was that of a hydrocephalic foetus where craniotomy and forceps delivery were performed.

There were 81 spontaneous deliveries in the series. Foetal distress, therefore, necessitated operative delivery in 24 cases out of 125 (19.2%), and this gives a rough indication of the risk these infants run.

The antenatal history of these cases has been investigated to see if there was any anoxia that might have produced temporary foetal distress, but there were only seven cases in which a possible relevant factor was found. In two cases external cephalic version under general anaesthesia was performed, while in another two cases version was attempted but was unsuccessful. One case had had mitral valvotomy performed during pregnancy, while two other cases had suffered from severe anti-partum anaemia—that is, haemoglobin of less than 50%. In a further two cases the cord was tightly round the neck of the foetus at birth, but the significance of this is doubtful. Shui and Eastman (1957) concluded that cord round the neck was not of significance as a cause of foetal distress, but Reiss (1958) feels that it is a factor of importance, late in labour at least.

The indications for which induction of labour was performed were next considered, to determine if there was any particular group of cases in which the foetal risk appeared to be high. As might be expected, prolongation of pregnancy was the principal indication in 75 cases. Thirteen of the 20 caesarean sections and 12 of the 18 deliveries by forceps were in this group, but these figures are in proportion and do not represent an unduly high incidence. Toxaemia of pregnancy was the indication in 17 of the cases, but five of the caesarean sections and three of the forceps deliveries were in this group. Although the total number of cases is small the number of caesarean sections is slightly higher than one would expect. Whether this high rate in toxaemia is justified is questionable, but it was felt that the combination of severe toxaemia and meconium-stained liquor was a particularly unfavourable one for the foetus. The remaining groups were small and no worthwhile conclusions can be drawn from them, but the various indications were: rhesus iso-immunization, contracted pelvis, previous caesarean section, ante-partum haemorrhage, foetal abnormality, unstable presentation, severe late vomiting of pregnancy, and breech presentation.

There were 117 babies born alive in this series, and in only one case did the baby show signs of serious asphyxia at birth which necessitated admission to the sick nursery. This was the baby which eventually died 6½ hours after birth. In no other case did the baby have a degree of asphyxia severe enough to necessitate admission to the nursery. Milder degrees of asphyxia undoubtedly occurred, but in a retrospective analysis such as this it is impossible to make an accurate assessment from the records, since there were a number of observers and no fixed standard of asphyxia which would permit a more detailed estimate.

It is also impossible to form any estimate of whether the degree of meconium staining gives an indication of the foetal prognosis, as there were several observers and again a definite standard is difficult to set up. This point requires further elucidation.

Discussion

Meconium staining of the liquor calls for a careful assessment of the case, with a study of all relevant factors such as maternal age, parity, obstetric history, reason for the induction of labour, and any associated toxaemia. In the absence of any specially unfavourable combination of these factors an expectant policy seems justified by the results obtained in this series. Nevertheless, such cases require to be watched very carefully, and the organization should be so directed that the initial warning signs of foetal distress will not be missed, as the appearance of these calls for immediate delivery. It follows that all such cases should be observed in an institution where caesarean section or forceps delivery can be quickly and easily performed.

In discussing the observation of these cases the papers of Lister and Buchanan (1957), and of De Soldenhoff and Brill (1954) on foetal distress are of interest. Lister and Buchanan concluded that if the major foetal heart changes are awaited the opportunity for active intervention may already have been lost. For this reason the lesser deviations in a foetal heart rate from a sustained level must also be considered in determining treatment, as they carry a significant increase in the incidence of asphyxia at birth. Variations in the foetal heart rate of 20 beats a minute or more may be significant in these cases. De Soldenhoff and Brill mentioned the importance of a foetal heart chart, as it is not the isolated reading that is so vital but the observation of a series of heart rates over a period which gives a more accurate picture. They also noted that the slowing of the foetal heart rate during a contraction was a warning sign of early foetal distress and not a normal finding.

The avoidance of prolonged labour in these cases is important. In this series the latent interval between the induction of labour and the onset of labour varied between 15 minutes and seven days, but there does not appear to be any relationship between the length of the latent interval and the length or type of labour which followed. In the case in which the latent interval was 7 days, labour lasted 7½ hours and ended in delivery by forceps on account of foetal distress; while in another case, in which the latent interval was only 2 hours, labour lasted 47½ hours and also ended in delivery by forceps. The length of labour has been investigated in the 114 cases which were treated expectantly at first, and it is significant that labour was completed in 24 hours in 80% of them. Lister and Buchanan showed that the incidence of foetal distress and asphyxia increased directly with the length of labour, and it may be that the good results in this series are in part due to the fact that labour was short in a high proportion of cases.

Conclusion

When meconium staining of the liquor is found at artificial rupture of the membranes an expectant policy is justified, but the presence of meconium is an alarm signal which calls for a careful assessment of the case by the obstetrician in charge, followed by unremitting vigilance to detect the early signs of definite foetal distress which would necessitate immediate delivery. A more radical policy as advocated by Walker does not appear to be necessary, since some warning of foetal distress by alteration in the foetal heart rate is invariably given. It should further be borne in mind that there is a considerable chance that a foetal

abnormality may be present and that a conservative policy may avoid caesarean section in these cases. The avoidance of prolonged labour is also important, and cases in labour longer than 24 hours call for reassessment if delivery is not imminent.

Even when an expectant policy is pursued, however, a high number of operative deliveries will still occur, so that these cases require the resources of a specialist maternity hospital. While this is in agreement with the views expressed by Macafee and Bancroft-Livingston, the problem of ante-partum meconium staining would seem to be more serious than they admit, since 19.2% of the cases in the present series required to be delivered by caesarean section or by forceps on account of foetal distress. It is not known whether serious asphyxia at birth is responsible for any impairment in subsequent mental ability, but there is much to be said in these cases for the view expressed by De Soldenhoff and Brill that the early signs of foetal distress must be observed and acted upon if maximum foetal salvage is to be secured.

Summary

Different views on the importance of meconium staining of the liquor amnii are presented, and a series of 125 cases in which ante-partum meconium staining was encountered is analysed.

An expectant policy is justified in most cases, but the incidence of foetal distress is greatly increased, as operative delivery was required on this account in 19.2% of cases.

Both the caesarean section rate and the forceps rate in the series were twice the hospital rate. These cases therefore require the resources of a specialist maternity hospital.

The importance of the recognition of the early signs of foetal distress in these cases is emphasized, as is also the avoidance of prolonged labour.

It is also noted that there is an increased incidence of an abnormal foetus in association with ante-partum meconium staining.

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THE SCHULTZ-DALE ANAPHYLACTIC TEST FOR CARCINOMA ANTIGEN

BY

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Makari and Huck (1955) and Makari (1958) have reported that a carcinoma antigen could be detected in the blood plasma of carcinoma patients. To detect the antigen they used the anaphylactic response of uteri from appropriately sensitized guinea-pigs described by Schultz (1910) and Dale (1913). Burrows (1958) has confirmed these findings. The work described below was an attempt to repeat these experiments.

Method

Human carcinomata were obtained at operation, and extracts were prepared as described by Makari and Huck (1955) and Makari (1956, personal communication). Homogenates were made in a rotary blender run at approximately 15,000 r.p.m. for 30 minutes, the blending container being packed in ice. They were then centrifuged at 3,000 r.p.m. (950 g) to remove debris. The supernatant from this centrifugation was recentrifuged at 10,000 r.p.m. (10,200 g) for 45 minutes, the precipitate being collected and stored at -20°C . This was the antigen to which guinea-pigs were to be sensitized.

Following the method of Makari and Huck, adjuvants were used with the object of increasing the sensitizing power of the antigen. The following modification of Freund's adjuvant was used:

"Bayol F"	8.5 ml.
"Arlacel A" special	1.5 ml.
<i>Mycobacterium tuberculosis</i>	5 mg. (steam-killed desiccated human bacilli)

These ingredients were mixed, an equal volume of a 20% suspension of antigen was added, and an emulsion was made in a glass blender.

Young virgin female guinea-pigs were given 1 ml. each of the emulsion by multiple subcutaneous inoculation. They were used for sensitivity tests between three and six weeks after inoculation.

Blood plasma for testing was obtained from patients with carcinoma and from normal subjects by venepuncture. A nylon syringe was used, and subsequently the blood and plasma were handled entirely in "polythene" or in siliconed glassware. Dry heparin was added and the blood cells were removed by centrifugation as soon as possible. The plasma was stored at $+4^{\circ}\text{C}$. for one to four days and was then divided into small samples, each sufficient for one test, and frozen to -20°C . It was allowed to thaw at room temperature just before it was needed. In the last two series of experiments the plasma was dialysed in "cellophane" against normal saline at $+4^{\circ}\text{C}$. for 24 hours, and soya bean trypsin inhibitor (S.T.I.) was added at a concentration of 1 mg./ml. before the plasma was frozen.

Blood plasma for desensitization of the uterus preparations was obtained from the human blood bank. Group O rhesus-positive blood was used. After removing the blood cells this plasma was also frozen