

probably little to be lost by starting them on admission in any severe attack, particularly if the child has previously required steroid therapy for asthma. There is no evidence that the liberal use of steroids in acute attacks alters the long term prognosis of the disease in any way.

- ¹ Godfrey, S., and Konig, P., *Archives of Disease in Childhood*, 1973, 48, 655.
- ² Frears, J. F., Wilson, L. C., and Friedman, M., *Archives of Disease in Childhood*, 1973, 48, 856.
- ³ *Postgraduate Medical Journal*, 1974, 50, Suppl. No. 4.
- ⁴ Williams, D. I., et al., *Lancet*, 1964, 1, 1177.
- ⁵ Sneddon, I. B., *British Medical Journal*, 1968, 1, 579.
- ⁶ Rook, A., Wilkinson, D. S., and Ebling, F. J. G., *Textbook of Dermatology*. Oxford, Blackwell, 1973.
- ⁷ McAllen, M. K., Kochanowski, S. J., and Shaw, K. M., *British Medical Journal*, 1974, 1, 171.
- ⁸ Friedman, M., and Strang, L. B., *Lancet*, 1966, 2, 568.

Antenatal Diagnosis of Spina Bifida

The antenatal diagnosis of spina bifida cystica can now be made by the measurement of alphafetoprotein (AFP) in amniotic fluid. Though only about 25 AFP assays in amniotic fluid have been reported from pregnancies with spina bifida, in all cases with "open" lesions (exposure of neural tissue to amniotic fluid) the AFP was above the highest normal value for the gestational age, usually by a substantial margin.¹⁻⁷ Anencephaly produced similarly high values, but closed spina bifida lesions, which account for about 15% of all cases,⁸ have been reported with normal levels. AFP is synthesized by the fetal liver and yolk sac,^{9 10} but the route by which it reaches the amniotic fluid is not known.

The specificity of amniotic fluid AFP measurement during the second trimester of pregnancy for the diagnosis of anencephaly and spina bifida has not been precisely determined. On present evidence false-positive results seem to be relatively rare. Occasionally levels are high in cases of fetal death.¹¹ High levels have been reported in cases of Turner's syndrome in which amniotic fluid was obtained from the products of conception after spontaneous abortion,¹² though in one case tested *in utero*¹¹ the level was only slightly raised.

Other methods of antenatal diagnosis have been described. Direct inspection of the fetus through a fiberoptic telescope has been tried but largely abandoned.¹³ A single case of occipital meningocele was detected by ultrasound scanning of a fetus at 16 weeks gestation,¹⁴ but the technique is time-consuming and difficult; its value still has to be established in routine practice. More recent diagnostic methods, such as measurement of beta-trace protein (a cerebrospinal fluid protein) in amniotic fluid¹⁵ or the macrophage content of amniotic fluid cells,¹⁶ have not yet been evaluated.

The diagnosis of spina bifida in the first half of pregnancy requires amniocentesis. Clearly this is not practical for screening the general population, though it is useful for screening women who have previously had one or more infants with a neural tube defect, since the risk of recurrence is about 1 in 20 after the first affected child and about 1 in 10 after the second.¹⁷ The increased risks of spina bifida associated with other factors such as poor social circumstances or residence in areas with a high incidence of the disorder are too small alone to justify routine amniocentesis.

Over 90% of infants with spina bifida are, however, born to women who have not previously had affected children, and for these another method of screening is needed. Though initial reports were discouraging,^{18 19} it has now been established that a high maternal serum AFP in early pregnancy is

commonly associated with spina bifida and anencephaly.^{20 21} Screening all pregnant women by measurement of the serum level of AFP is, therefore, now possible—given the laboratory facilities—and should be followed in patients with high levels by ultrasonography to detect anencephaly and to exclude multiple pregnancy,²² and by amniocentesis to detect open spina bifida.

In Edinburgh and Oxford 27 mothers with fetuses affected by both types of spina bifida cystica (open and closed) have had their serum levels measured between 14 and 21 weeks gestation, and one-third had levels above the 98th percentile.²³

Some centres are already undertaking antenatal screening on a pilot basis, and a few pregnancies with spina bifida have been terminated. However, many of the practical and ethical problems associated with antenatal screening and selective abortion after amniocentesis are unsolved.^{24 25} The timing of the AFP measurement for optimal discrimination between affected and unaffected pregnancies is not yet known. The risks of amniocentesis have not yet been fully quantified, and it is not known how high the maternal serum AFP must be before these risks will be outweighed by the possible benefits of interrupting a pregnancy with spina bifida. This decision is of some importance, since the number of amniocenteses performed will substantially exceed the number of potentially viable infants detected with spina bifida. If amniocentesis is restricted to the 2% of singleton pregnancies with the highest maternal serum AFP levels, 1 in 20 will have a fetus with spina bifida without anencephaly and a further 1 in 20 will have one with anencephaly. The risk in this group is thus higher than that in patients with a previously affected child, where amniocentesis is already considered acceptable. In Britain, with nearly 800 000 births a year, such screening would lead to an annual total of 16 000 amniocenteses and might detect about one-third of the 2400 infants with spina bifida. About half of these die at or shortly after birth,⁸ but of the remainder who survive only about a quarter are ambulant, continent, and free from mental handicap.

It is a major advance to be able to identify and offer to terminate 800 pregnancies with spina bifida each year, 300 of which would result in children who grew up seriously handicapped. Unless the risks of amniocentesis in the second trimester of pregnancy prove to be unexpectedly high, general antenatal screening for spina bifida may now be seriously considered.

- ¹ Brock, D. J. H., and Scrimgeour, J. B., *Lancet*, 1972, 2, 1252.
- ² Lorber, J., Stewart, C. R., and Milford Ward, A., *Lancet*, 1973, 1, 1187.
- ³ Seller, M. J., et al., *Lancet*, 1973, 2, 73.
- ⁴ Allan, L. D., et al., *Lancet*, 1973, 2, 522.
- ⁵ Nevin, N. C., Nesbitt, S., and Thompson, W., *Lancet*, 1973, 1, 1383.
- ⁶ Brock, D. J. H., and Scrimgeour, J. B., *Lancet*, 1974, 1, 569.
- ⁷ Nevin, N. C., Thompson, W., and Nesbitt, S., *Journal of Obstetrics and Gynaecology of the British Commonwealth*, 1974, 81, 757.
- ⁸ Laurence, K. M., *Lancet*, 1974, 1, 301.
- ⁹ Gitlin, D., and Perricelli, A., *Nature*, 1970, 228, 995.
- ¹⁰ Gitlin, D., and Boesman, M., *Journal of Clinical Investigation*, 1966, 45, 1826.
- ¹¹ Milunsky, A., and Alpert, E., *Journal of Pediatrics*, 1974, 84, 889.
- ¹² Seller, M. J., Creasy, M. R., and Alberman, E. D., *British Medical Journal*, 1974, 2, 524.
- ¹³ Scrimgeour, J. B., *Antenatal Diagnosis of Genetic Disease*, ed. A. E. H. Emery, Edinburgh, Livingstone-Churchill, 1973.
- ¹⁴ Campbell, S., from *Birth Defects*, ed. A. G. Motulsky and W. Lenz. International Congress Series no. 310, p. 240, Amsterdam, Excerpta Medica, 1974.
- ¹⁵ Macri, J. N., Weiss, R. R., and Joshi, M. S., *Lancet*, 1974, 1, 1109.
- ¹⁶ Brock, D. J. H., Unpublished observations.
- ¹⁷ Leck, I., *British Medical Bulletin*, 1974, 30, 158.
- ¹⁸ Seller, M. J., et al., *Lancet*, 1974, 1, 428.
- ¹⁹ Harris, R., et al., *Lancet*, 1974, 1, 429.
- ²⁰ Wald, N. J., Brock, D. J. H., and Bonnar, J., *Lancet*, 1974, 1, 765.
- ²¹ Brock, D. J. H., Bolton, A. E., and Scrimgeour, J. B., *Lancet*, 1974, 1, 767.
- ²² Wald, N. J., et al., *British Medical Journal*, 1975, in press.
- ²³ Brock, D. J. H., and Wald, N. J., Unpublished observations.
- ²⁴ Jones, A., and Bodmer, W. F., *Our Future Inheritance: Choice or Chance?* London, Oxford University Press, 1974.
- ²⁵ *British Medical Journal*, 1974, 4, 676.