highest risk of recurrence, but cumulative recurrence rates were similar after the first three operations. Sixteen of 34 deaths were attributed directly to Crohn's disease, most of the "avoidable" deaths occurring before 1966.

The Birmingham results are inevitably a personal series, using the particular medical and surgical approach of one team. The periods of observation, however, are so long that even better results might be expected in today's patients: metronidazole has transformed sepsis after colonic surgery and parenteral nutrition can help the catabolic patient with a damaged small bowel. Though the patients with Crohn's disease in this series were at some increased risk, especially early in their illness or from rare gastrointestinal malignancy, most were able to enjoy a full life despite their illness.

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Thomas Lewis and clinical research

On his tombstone Sir Thomas Lewis (1881-1945) is described as "physician and scientist," and, indeed, one of his beliefs was that clinical science should be differentiated from the practice of medicine. While this philosophical concept is still debated there can be no argument about his contributions to cardiology in particular and to medicine in general.

Having studied in Cardiff and qualified from University College Hospital, London, in 1905, Lewis plunged into research as well as clinical work. He was largely responsible for introducing the electrocardiograph into clinical use, and it is a daunting thought that Lewis could master this tool so that within a decade he had categorised the features of most cardiac arrhythmias. Furthermore, within five years of qualifying he had established *Heart*, forerunner of *Clinical Science*, which he later handed over to the Medical Research Society. Indeed, this society, the forum where so many young research workers present their work, was his creation, and as one of the founder members of the Cardiac Club in 1922 he helped establish its successor, the British Cardiac Society.

Lewis's contributions were by no means confined to electrocardiography and the study of cardiac rhythms, or indeed other aspects of cardiology. In the 1920s and 1930s he turned his attention to the peripheral circulation and to the mechanisms of pain and wrote extensively on the philosophy of clinical science. Nevertheless, his best-known contributions were to scientific cardiology. He had wide influence abroad, especially in the United States; one of his American disciples, the late Samuel Levine, endowed the Thomas Lewis Lecture of the British Cardiac Society in his memory.

Lewis was a vigorous and original worker whose writings still repay rereading. On 24 April a symposium at the Wellcome Institute for the History of Medicine was devoted to him and his work, and an associated exhibition remains open there until 29 May. He died in 1945, 18 years after the first symptoms of coronary heart disease appeared. Lewis had a long association with University College Hospital and the Medical Research Council and is still personally remembered by many, but his influence is also maintained by several of his books: all who work on cardiac arrhythmias recognise the fundamental importance of *The Mechanism and Graphic Registration of the Heart Beat*, published in 1925.[1] Not only was he an original medical scientist whose practical contributions remain of value: today's clinical scientist owes much to the recognition that he receives to the impetus of Sir Thomas Lewis.

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Regular Review

New uncertainties in prenatal screening for neural tube defect

RODNEY HARRIS, A P READ

Two years ago a working group under the chairmanship of Sir Douglas Black[1 2] advised on "what guidance might be given to health authorities on the introduction into routine antenatal care of a service to detect neural tube defects." Its report concentrated on one method—screening by measurement of alphafetoprotein in the maternal serum. In retrospect, the report may be seen to have marked the end of a stage in the development of screening for neural tube defect, since it did not advocate immediate provision for all pregnancies and it preceded several important developments. The time is now ripe for a re-evaluation of procedures for the detection and prevention of fetal neural tube defect.

To obstetricians the most impressive new factor is the improved resolving power of diagnostic ultrasound.[3 4] Screening by ultrasound has become a serious alternative to screening by maternal alphafetoprotein. Examination of a fetus by high-

resolution diagnostic ultrasound is being claimed to be capable of identifying all but a minority of spina bifidas between 16 and 20 weeks of gestation,[4] apparently without the result of alphafetoprotein estimation to point the way. The ultrasound technique misses between 5% and 10% of spina bifidas; maternal obesity may be one reason for poor scans. The neural tube defects missed are, however, often low in the lumbar spine, and in the absence of associated cerebral ventricular dilatation the prognosis is likely to be better than for higher lumbar and dorsal lesions. This reported false-negative rate compares favourably with the figure for screening by maternal alphafetoprotein, which is at least 20%.[1]

With the right equipment in skilled hands high-resolution diagnostic ultrasound can also diagnose many other malformations, some of which have no effect on maternal alphafetoprotein. These include closed neural tube defect, abdominal wall defects, polycystic disease of the kidney, renal agenesis, congenital heart lesions, and short-limbed dwarfism.[4] One anecdotal report[5] has even suggested that measurement of the cephalic index (ratio of occipitofrontal to biparietal diameter) by high-resolution diagnostic ultrasound at 16 to 20 weeks may be able to identify some unsuspected fetuses with Down's syndrome. Although we are not yet aware of any data from measurements in utero confirming this remarkable observation, Dr Hylton Meire (personal communication) has measured the cephalic index of eight fetuses with Down's syndrome after termination at 20 weeks. All had indices below those measured on a number of aborted normal fetuses of the same gestational age. If further substantiated this would provide an important advance in prenatal screening. Some 70% of babies with Down's syndrome are born to women aged under 35, though the overall incidence in this younger group is about 0·1% compared with 1% in 40-year-olds. Thus if high-resolution diagnostic ultrasound could define a 10% subgroup of these younger mothers which included all those with Down's fetuses amniocentesis would become cost effective and a major impact could be made on the incidence of Down's syndrome.

A second important development is the introduction of a new diagnostic technique employing qualitative electrophoresis of acetylcholinesterase in amniotic fluid. This has proved to be a most valuable adjunct to the use of amniotic alphafetoprotein estimations in the prenatal diagnosis of neural tube defect.[6–8] Combined use of the two tests yields more information than either test used alone. When concentrations of both alphafetoprotein and acetylcholinesterase are raised in amniotic fluids false-positive predictions of neural tube defect are virtually excluded. A few fetuses with false-negative alphafetoprotein will be detected by the characteristic second band on the acetylcholinesterase gel, though the diagnosis would require confirmation by high-resolution diagnostic ultrasound before termination of pregnancy could be recommended. Fetuses with raised alphafetoprotein but normal acetylcholinesterase (or only a faint second band) are likely to have exomphalos, gastroschisis, kidney defects, or a variety of other abnormalities, some of which are surgically correctable—and the abortion of fetuses with correctable defects should not be dismissed as an unimportant side effect of maternal serum alphafetoprotein screening.

Increasingly, screening for neural tube defect entails low-incidence populations, because the general incidence of neural tube defect appears to be falling. Birth notifications in England and Wales of infants with malformations of the central nervous system fell from 37·9 per 10 000 in 1974 to 32·5 in 1976 (the year quoted in the Black Report[1]) and to 25·5 in 1979.[9] Since these figures are based on live births as well as stillbirths but do not include aborted fetuses the downward trend may (to some extent) reflect the success of screening. Follow-up of pregnancies screened by maternal alphafetoprotein in the north-west of England has also suggested a low incidence of neural tube defect, with in some cases twice as many anencephalics as spina bifidas (D Orrell, personal communication). Well-organised screening programmes include such follow-up, but necessarily it has to be limited to positive predictions; the numbers are too high for confidence that all the false-negatives could be identified. The unexpectedly low number of spina bifidas detected might be due either to the low sensitivity of screening by maternal alphafetoprotein or to a true fall in incidence. Irrespective of the cause, the implications are unfavourable for the costs and benefits of screening whose main or only target is neural tube defect, since, as the number of such fetuses detected falls, the financial costs and the numbers both of false-positives and of fetuses harmed remain static.

Another development is the possibility of prevention. The incidence of neural tube defect could be reduced further if periconceptional vitamin supplementation is shown to go some way towards primary prevention of neural tube defect.[10] Nevertheless, vitamin supplementation would be unlikely to prevent all neural tube defects, partly because it would be impossible to supplement all women, and also because the causes of neural tube defect are heterogeneous. Screening of some sort would therefore continue to be required, but the method used would have to be appropriate for populations with a low incidence of neural tube defect.

The remarkable technical advances in high-resolution diagnostic ultrasound, uncertainties about the efficiency of screening by estimating maternal alphafetoprotein concentrations, and the prospect of having to screen populations with an incidence of neural tube defect below the range of two to six per 1000 total births considered by the Black Report all require that we take a new look at prenatal screening for neural tube defect. Once amniotic fluid has been obtained, the combination of alphafetoprotein, acetylcholinesterase, and high-resolution diagnostic ultrasound assures great diagnostic accuracy, but amniocentesis is appropriate only for pregnancies already known to be at high risk of fetal malformation. The main problem, therefore, is to select the most appropriate general screening test for defining these high-risk pregnancies.

Ultrasonography is already an essential component of screening by maternal alphafetoprotein estimations. The Black Report allocated to ultrasound 7% of the revenue and 14% of the capital cost of a national screening programme on the assumption that 30% of women would need scanning to establish gestational age, 3% for placental location and detection of multiple pregnancy, and 0·2% high-resolution diagnostic ultrasound for the diagnosis of open neural tube defect.[1] In the two years since the publication of the report, however, high-resolution diagnostic ultrasound has acquired greater potential as a screening technique. Versatile, relatively quick, and apparently safe, in an ideal world it might immediately replace estimating maternal serum alphafetoprotein as the main method for detecting fetal defect. If ultrasound diagnosis of Down's syndrome or some of the other defects mentioned above proves practicable for population screening the arguments for a central role for high resolution diagnostic ultrasound seem irresistible. Moreover, rapid advances are being made in both technology and skill, so that today's best results could soon be routine. Maternal serum alphafetoprotein estimations have some additional uses in the diagnosis of

fetal abnormality and at-risk pregnancies,[2] but their versatility does not compare favourably with high-resolution diagnostic ultrasound.

The safety of ultrasound as a population screening measure should be periodically reviewed, though there is no evidence of harm from diagnostic ultrasound in the doses used.[4] Informed consent should be obtained before screening. This matter may not, perhaps, have received sufficient attention in all the centres offering screening by maternal alphafetoprotein estimations, and when all patients have ultrasound scans as part of their routine antenatal care it may prove difficult to avoid the consequences of the accidental discovery of fetal malformation. Instant feedback to the mother (usually an interested participant in high-resolution diagnostic ultrasound) could prove a disadvantage. On the other hand, women now suffer stress during screening by maternal alphafetoprotein estimation while waiting for results,[11 12] and the immediacy of high-resolution diagnostic ultrasound can be used to minimise this.

Though equipment for high-resolution diagnostic ultrasound is not excessively expensive and might be provided fairly quickly, the skills required are restricted to a few centres, and the service could not easily be expanded rapidly to provide high-resolution diagnostic ultrasound for all pregnancies for the detection of fetal defect at 16-18 weeks, although this has been achieved in a few places (A D Christie, W G Miller, and J G Donald, 22nd British Congress of Obstetrics and Gynaecology, 1980). In part the problem stems from the new and fully justified popularity of ultrasonography and CT scans. These techniques are valuable in most clinical disciplines, so that obstetric ultrasound has to be considered in the context of rapidly growing demands for diagnostic imaging generally. Medical skills and technical advances have already outstripped the ability of the Health Service to fund them, and as always the question is one of priorities. The provision of adequate obstetric high-resolution diagnostic ultrasound has a high claim. The distress caused by the abortion of a wanted, normal pregnancy or damage to a normal fetus by amniocentesis is acceptable and ethically justifiable only if we are sure that we have applied the very best diagnostic procedures available. Furthermore, planners should be aware that this is preventive medicine—in the sense that a great deal of money is saved in the long run by not having to provide for the long-term management of mentally and physically handicapped persons.[13 14]

We believe that there is an unanswerable case for high-resolution diagnostic ultrasound being available in at least one centre in each region to cope with the relatively small number of difficult diagnostic problems generated by present screening programmes. Official policy on prenatal screening needs urgent reappraisal with the following chief aims:

(1) Comparison of the relative merits of screening by maternal alphafetoprotein estimations and by high-resolution diagnostic ultrasound in terms of safety, feasibility, accuracy, versatility, and consumer acceptability. Comparative costings are needed of screening programmes based on the two techniques.

(2) Examining ways of integrating screening, diagnosis, and care so as to reduce to a minimum the medical, social, and ethical problems of prenatal diagnosis and the termination of wanted pregnancies.

(3) Improving epidemiological data on fetal neural tube defect, which is essential if the effect of present and future screening programmes, secular changes, and any fall in the prevalence of neural tube defect from dietary supplementation are to be measured.

We are grateful to Drs Dian and Paul Donnai for helpful comments, and to Mrs Mae Kaul and Mrs K Winkle for secretarial help.

RODNEY HARRIS
Professor

A P READ
Lecturer

Department of Medical Genetics,
St Mary's Hospital,
Manchester M13 0JH

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