Abstracts of the Joint Meeting of the Clinical Genetics Society and the Royal College of Obstetricians and Gynaecologists held at the Royal College, London, on 27 October 1982

Genetic aspects of infertility (with special reference to AID)

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Chromosomal abnormalities make a significant contribution to male infertility, the majority asserting their effect through gametogenic impairment. A clinical examination and semen analysis should allow a selection of cases for more detailed genetic assessment. The identification of an irreversible cause of infertility, such as Klinefelter's syndrome, may make further invasive investigative procedures unnecessary. In contrast, genetic causes of female infertility are rare. An affected female can present with amenorrhoea and absence of apparent somatic abnormalities. Chromosomal analysis should be performed on all such patients and particularly in those with raised gonadotrophin levels. In the United Kingdom, as elsewhere, there has been an upsurge in the practice of AID mainly attributed to changes in social attitudes; at least 3000 patients are now treated annually. The confidential nature of the practice of AID has curtailed the follow-up of many such pregnancies, but the outcome of a confidential enquiry undertaken by the Royal College of Obstetricians and Gynaecologists since 1977 suggests an extremely low incidence of congenital abnormalities. A genetic disorder in which there is a high risk of serious abnormalities or disease being transmitted from father to offspring can be treated by AID. Male chromosomal abnormalities causing infertility can be dealt with in a similar manner. The secrecy surrounding the AID child could present the geneticist with difficulty if it became necessary on clinical grounds to investigate hereditary diseases.

Chromosomal analysis of couples with repeated spontaneous abortions

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Chromosome banding studies were carried out on both partners of 182 consecutive couples with a history of two or more spontaneous abortions. Seventeen abnormal karyotypes were detected. This represents a frequency of 4.67%. The pregnancy outcome in 105 couples with normal and abnormal karyotypes was compared. The distribution of confirmed pregnancies, confirmed spontaneous abortions, live-births, still-births, ectopic gestation, and medically induced abortion was not significantly different in the two groups. It is reasonable to postulate a genetic basis for recurrent abortion and the clinician looks forward to the development of further techniques in genetic investigation which could differentiate between those couples with a bad pregnancy pattern and those in whom a more favourable outcome can be expected.

Familial ovarian cancer: gynaecological and genetic management

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A large family was identified in which ovarian cancer is segregating as a dominant trait. Forty-two female members were found to have a 1 in 8 or greater risk of developing the disease. A joint gynaecological/genetic clinic was set up to advise and examine members of the family. Of the 42 females at high risk, 18 attended the clinic; 19 were under the age of 15 and their mothers were counselled; two were alive and well over the age of 65 years; one was abroad, and only one woman at high risk who had a young daughter refused the invitation to the clinic. Five women have had prophylactic oophorectomy and several more intend to request the procedure when their families are complete. Problems of ascertainment and management of the family were discussed together with a review of relevant literature.

Obstetric and gynaecological problems in women with chondrodystrophies

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In recent years there has been a great deal of interest in distinguishing various types of chondrodystrophies. There has been a growing body of knowledge about the natural history of various types. However, little is known about obstetrical and gynaecological complications. For this reason we undertook a survey in cooperation with Little People of America to establish the incidence of obstetrical and gynaecological problems in dwarfed
women. We questioned over 150 women, representing more than ten specific chondrodystrophies. Our data indicate an increased incidence of menstrual irregularities in all dwarfed women. Achondroplastic women appear to have early puberty, premature menopause, and an increased incidence of fibroids. Various types of contraception are associated with problems such as establishing correct dosage of oral agents and ease of use of diaphragms. Less than half the married women became pregnant, suggesting reduced fertility. However, pregnancy is surprisingly well tolerated. Delivery is almost always by Caesarian section; general anaesthesia is usually indicated because of vertebral anomalies. However, a number of unusual specific complications have been observed with pregnancy and delivery.

Preconceptional counselling
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Antenatal care is well established in the western world. However, it usually starts after the first few weeks of gestation have passed. It is therefore of little use in preventing teratogenesis. Further, there may be merit in treating the parents before pregnancy to ensure the conception occurs in the best physiological conditions. There are certainly good reasons for counselling couples before the woman becomes pregnant about the recurrence of any previous obstetrical hazards.

A prospective view of genetic counselling
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Fifty-two consecutive referrals for genetic counselling were studied prospectively. Couples were interviewed before the counselling session, immediately after it, and 3 months later at home. The counsellors filled in a questionnaire after each counselling session. Most couples knew what they wished to learn from genetic counselling, but some were bewildered by not knowing what the session would consist of. About half already had broadly correct risk information before the session, and four-fifths remembered the risk correctly at 3 months. One quarter of the couples altered their plans for or against a further child over the study period. Most couples appeared to be using information on risk and prognosis to reach a decision, but other important factors in their decisions, which had not emerged during the counselling session, became obvious at the home visits.

Early genetic counselling and its effect on amniocentesis referral
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A total of 425 women was referred in the first trimester of pregnancy for genetic counselling with a view to amniocentesis. These included patients with a high risk for neural tube defects, chromosomal abnormalities, maternal age, and other genetic diseases. The referral rate for amniocentesis was extremely low following genetic counselling: 23% for the NTD group, 21% for maternal age, and 7-3% in the chromosome abnormality group. When amniocentesis was not performed the appropriate screening procedure was undertaken, for example, serum AFP for NTD, blood for chromosomes for translocation carriers, or ultrasound scanning for skeletal abnormalities. It seems that genetic counselling in early pregnancy reduces the number of women who actually proceed to amniocentesis.

Genetic counselling for couples at high risk for neural tube defect during pregnancy. Is this the best time to attend?
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Home visits were made in 1981 to 49 women who had been seen in 1977 or 1978 by KML for genetic counselling only during an 'at risk' pregnancy. The reasons for this late attendance were studied. The majority were already aware of their possible risk and of the availability of antenatal diagnosis tests. But many did not know the precise likelihood of their own pregnancy being affected and did not know that the amniocentesis could precipitate a miscarriage or that the tests could fail to detect some affected fetuses. The women found the genetic counselling session helpful and the majority felt happy to take the decision about amniocentesis themselves. Forty-six had an amniocentesis, one woman miscarried, and two had termination of a pregnancy, the fetus having a neural tube defect. All the couples found the weeks waiting for the results of laboratory tests distressing. The couples' further child-bearing plans took into account the increased emotional trauma for them of a pregnancy. The actual risk of recurrence did not seem to enter into the decision as only a minority had a clear recollection of the recurrence risk figure given. The 25 who planned more children intended to use the antenatal diagnosis service again.

The impact of maternal serum AFP screening on antenatal diagnosis
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One way of assessing the impact of maternal serum AFP screening is to compare the yield of abnormal fetuses detected with the yield found from other indications for amniocentesis. An analysis of this type has been made for the Edinburgh area in the years 1979 and 1981. As a result of 2137 amniocenteses there were 104 terminations of pregnancy, 66 of which (63%) followed from a raised
maternal serum AFP indication. Even when anencephaly was excluded from the analysis, maternal serum AFP was responsible for detecting 35 out of the 63 (56%) abnormal fetuses. Such data constitute a strong case for continuation of serum AFP screening programmes.

The potential use of fetal liver biopsy
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It is now possible to diagnose this X linked urea cycle defect on fetal liver taken via the fetoscope at 18 to 20 weeks' gestation. The enzyme is not expressed in amniotic cells, and studies on control fetal material shows that the enzyme activity develops in fetal liver between 15 and 17 weeks. Three pregnancies are described in which the mother is a known carrier. All the fetuses were male. The first showed undetectable OCT activity and the diagnosis was confirmed after termination of the pregnancy; the second had normal levels and the boy is clinically and metabolically normal at one year; and the third is being carried out in August 1982. Some female carriers have significant hyperammonaemia and mental retardation. It is possible that maternal hyperammonaemia may damage a heterozygous female fetus in utero, and this calls for special management of the pregnancy, particularly if the mother is on a low protein diet.

Trophoblast sampling in early pregnancy; evaluation of an endocervical aspiration biopsy technique
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The reliability and frequency of obtaining chorionic villi by endocervical aspiration has been studied with a view to using this technique to obtain fetal cells for antenatal diagnosis. A total of 65 samples from 33 women was obtained by blind endocervical aspiration (St Mary's group) and 49 from 19 women were obtained by endocervical aspiration under ultrasound control (UCH group). Data were obtained on parity, gravidity, endocervical canal length, and cavity length and the gestational age was carefully calculated. Villus content of the aspirates was determined by phase contrast microscopy of fresh samples and by histological analysis of paraffin embedded tissue. Villus material was present in samples from 18 of 33 women (54%) in the St Mary's group and in 12 of 19 women (63%) in the UCH group, showing that the use of ultrasound improves the success rate. The combined results from both groups showed that no villi could be obtained at 6 and 13 weeks' gestation. The aspiration was most successful at 9 weeks when samples from five of six women (83%) contained villi.

The outcome of pregnancy following unexpected chromosomal changes
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So far we have performed 2050 amniotic fluid cultures in pregnancies at risk for chromosomal imbalance, metabolic disorders, or neural tube defects. Out of these, 3% turned out to have pathological findings (trisomy 21, trisomy 18, trisomy 13, pathological AFP values and so on). Particularly in the field of cytogenetics, however, one has to come to terms with another 3% of unexpected karyotypes, which though being abnormal do not necessarily cause a pattern of developmental defects (marker chromosomes, balanced de novo translocations, inversions, mosaicism, or abnormal sex chromosome patterns). By means of some unexpected chromosomal changes observed antenatally by us, we discuss the proceedings in unexpected fetal chromosomal changes. We present evidence that in chromosomal aberrations like those cited above, termination of the pregnancy is not the only possibility to be considered.

The legal implications of antenatal screening and diagnosis
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In order to understand the legal implications one has to consider the ways in which the Courts assess the standard of the legal duty of care and the persons to whom that duty is owed. In making the assessment the Court has regard not only to current practice in different types of unit, but also to the availability of necessary scientific equipment. In new fields of medicine and surgery the medical profession is going through a period of setting its own standards of what is adequate treatment and Judges are, in the main, having regard to what the profession is doing rather than endeavouring to create any 'ideal' standard, which for lack of training facilities or economic resources cannot be achieved in some units. In considering the persons to whom the duty is owed, the Law has so far tended to treat husband and wife on an equal footing because the Law is geared to compensation in money terms. However, there is an expanding volume of decisions, many of which are difficult to interpret, as to how far a person who has himself suffered no physical injury can recover compensation for "emotional" injury. The duty of care (if any) owed to the fetus which is not delivered presents no current legal problem, but that owed to the child who is born following negligent screening or the negligent absence of screening is a matter of serious legal debate. There have been a few legal decisions which are pointers, but as they conflict with views held 10 years ago by Lawyers who are now High Court Judges it would be foolish to say that there is any degree of certainty in the long term about the outcome of such claims.
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