Some medical problems in pregnancy

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Pregnancy is an elegant masterpiece of physiological adjustment and as such is well tolerated by most healthy women. When the tenuous divide between the physiological and pathological state breaks down, however, it can become for the mother and her foetus a life-threatening event calling for skilled obstetrical and medical management. One of the more significant events contributing to improved maternal and foetal well-being in the last half-century has been closer cooperation between the general practitioner, the obstetrician, and the paediatrician with the medical and surgical specialist accepting an active role in the management team. This combined approach is essential to the successful outcome of pregnancy complicated by a medical disorder.

In this review I have selected a few of the many medical problems which can threaten pregnancy — the choice is personal, and by no means comprehensive.

Hypertension in pregnancy

When a pregnant woman presents with hypertension, two questions need to be answered: first, does the patient definitely have sustained, rather than casual elevation of blood pressure, and if so how severe is this?; and second, is the blood pressure elevation induced by the pregnancy (pre-eclampsia), or is it a result of another disease, most commonly so-called essential hypertension? — in which case the prognosis for both the mother and foetus will be very much better. As in the non-pregnant state, the general cardiovascular status of the patient is more important than the mere height of the blood pressure which, when estimated by sphygmomanometry, gives at best an inaccurate assessment of the arterial pressure. A previous history of elevated blood pressure will favour a diagnosis of essential hypertension, but in the second half of pregnancy pre-eclampsia may be superimposed on long-standing hypertension. Premonitory symptoms, such as headaches, visual disturbance, epigastric pain and vomiting, and the appearance of albuminuria can indicate the onset of fulminating pre-eclampsia (Matthews *et al.*, 1978), but the most sensitive indicator for developing pre-eclampsia, and for foetal survival, is elevation of the plasma

urate (Redman *et al.*, 1976). The prognosis for the foetus is directly related to the stage of the pregnancy at which pre-eclampsia develops — the earlier the onset, the worse the outlook.

Patients with well controlled non-albuminuric hypertension may be managed as outpatients. Women with persistent elevation of blood pressure above 140/90mmHg should be observed carefully during pregnancy, and those with persistent elevation of blood pressure above 170/110mmHg should receive treatment with anti-hypertensive drugs. The most popular anti-hypertensive drug in pregnancy is methyldopa, (Redman *et al.*, 1977), with hydrallazine being added if necessary. A recent report (Tcherdakoff *et al.*, 1978) suggests that propranolol may be well tolerated in pregnancy. Diuretics have the disadvantage of elevating the maternal plasma urate thereby removing a sensitive measure of foetal progress. Patients should be carefully assessed after pregnancy to determine if long-term management of hypertension will be necessary.

Diabetes mellitus

In the early part of this century diabetes mellitus was associated with a maternal mortality of nearly 30% and a perinatal loss of 50%. These appalling figures have now been reduced to a zero maternal mortality, with a foetal loss of around 5% (Drury, 1978) which is none the less considerably higher than that for non-diabetic mothers.

Diabetes should be suspected when there is a family history, especially in first degree relatives, glucose in a 'second fasting' urine sample (glycosuria is common in pregnancy but the accuracy of this test is increased if the urine voided on waking is discarded, and a fresh specimen passed fifteen minutes later while still fasting is tested); a history of unexplained perinatal loss, a 'large for dates' infant, or a malformed infant, gross maternal obesity; and, perhaps, of lesser significance, parity greater than five, recurrent toxaemia of pregnancy, and recurrent premature labour (Drury, 1978). Diabetes may appear for the first time in pregnancy — gestational diabetes.

Once diabetes has been diagnosed, the aim of all involved in management is the strict maintenance of normal blood sugar levels. Insulin, when indicated, is given in a dosage sufficient to keep the blood glucose levels at 5.5mmol/l (11mg/100ml) in the fasting state and 7.7mmol/l (140mg/100ml) after a meal. The timing of delivery is carefully planned by the managing team and, as the respiratory distress syndrome is a major cause of foetal mortality, tests of foetal lung maturity, such as the lecithin-sphingomyelin ratio in the amniotic fluid, are of considerable importance in reducing foetal loss (Drury, 1978).

Venous thrombosis and pulmonary embolism

Venous thrombosis is common in pregnancy, and pulmonary embolism is second only to abortion as a cause of maternal mortality (Report on Confidential enquiries into Maternal Deaths in England and Wales, 1970-1972 [DHSS, 1975]), but frightening as this statistic may sound when put in this way, it must be remembered that pulmonary embolism only causes death in two to three mothers in every 100,000 maternities, and this small risk must be carefully balanced against the dangers of anticoagulant treatment during pregnancy. In pregnancy there is the problem, on the one hand, of detecting the mother at risk from thromboembolism who may need prophylactic anticoagulant therapy and, on the other, the difficulty of diagnosing with accuracy an acute venous thrombosis or pulmonary embolism.

Risk factors, such as a previous history of thromboembolism, especially in pregnancy or with anovulant preparations, the presence of associated illness (diabetes, cardiac disease, hypertension or toxaemia), obesity, immobility, advanced age, high parity, blood group other than O and a planned caesarean section, need to be carefully assessed. Oral anticoagulants are best avoided in pregnancy because of the risk of teratogenicity and foetal haemorrhage (Bonnar, 1976). Heparin, which has a large molecular weight, does not cross the placental barrier and can be self-administered by subcutaneous injection (Bonnar, 1976; Spearing *et al.*, 1978). However, there are disadvantages with

heparin — it is costly, the injections are inconvenient and uncomforable for the patient, haemorrhagic complications may occur if there are not facilities for careful haematological control, and epidural anaesthesia is contraindicated. The decision to prescribe heparin, perhaps for most of pregnancy, must therefore be based on sound criteria.

Heart Disease

Clinical effects of the physiological changes in pregnancy

The resting cardiac output increases by about 40% early in pregnancy and this increase is maintained throughout pregnancy and into the puerperium. There is also a redistribution of peripheral blood flow, with increases in renal, skin and uterine flow, and the total blood volume increases by around 50%. There is a decrease in pulmonary and systemic vascular resistance which at least may partly explain the tendency to fainting in the normal woman or to pulmonary oedema in women with mitral stenosis (Conradsson and Werkö, 1974).

These haemodynamic alterations in themselves may produce clinical signs, or signs already present may be modified. Breathlessness is a common symptom during pregnancy, as is ankle oedema resulting from the high venous pressure in the legs, and cardiac failure may be misdiagnosed. The presence of basal crepitations due to compression of the basal parts of the lungs by a large uterus can make the diagnosis more difficult, and the jugular venous pressure and a chest x-ray may have to be carefully assessed. The heart occupies a more horizontal position, either making the apex beat more diffuse, or displacing it laterally; and radiologically the heart may appear enlarged.

On auscultation a third heart sound may be present in up to 90% of women, and in 10% a fourth heart sound may be heard. A physiological ejection murmur is common in the pulmonary area, and a murmur of similar quality may be present in the parasternal area in the fourth to sixth intercostal spaces — murmurs which can be confused with an atrial septal defect, mitral regurgitation, ventricular septal defect, or an obstructive cardioymopathy. A diastolic murmur, similar to the Graham-Steell murmur, may be heard over the pulmonary area and is due to physiological dilatation of the pulmonary artery, and occasionally a diastolic murmur may be heard over the tricuspid area due to increased blood flow — these murmurs can suggest a diagnosis of aortic or pulmonary regurgitation, or mitral stenosis. A venous hum is sometimes heard over the base of the heart and disappears when the jugular vein is compressed or when the patient lies down, and the mammary *souffle* or so-called *spargotic* murmur — a continuous murmur best heard in the parasternal area — is thought to be due to the increased flow in the mammary vessels, and disappears when pressure is applied to the stethoscope. These continuous murmurs may raise the suspicion of a patent ductus arteriosus. The hyperkinetic circulation of pregnancy can diminish the murmurs of aortic and mitral regurgitation, while increasing the intensity of mitral or tricuspid stenotic murmurs. (Conradson and Werkö, 1974).

The diagnosis of cardiac disease in pregnancy can be difficult, particularly if a number of auscultatory phenomena are present, and in many cases a firm diagnosis is not possible. Careful observation during pregnancy then becomes essential, with detailed reassessment in the puerperium to exclude or confirm the presence of organic cardiac disease.

Rheumatic heart disease

Although recent reviews (Szekely *et al.*, 1973; Conradsson and Werkö, 1974) show a gradual decline in both the incidence and severity of rheumatic heart disease, it remains a serious medical risk in pregnancy being the most common form of heart disease in many countries. Mitral stenosis, either pure or combined with regurgitation, is the most common of all rheumatic valvular lesions. Because of the difficulty of applying a functional grading in pregnancy it is best to base antenatal assessment on objective findings. The most serious complications are acute pulmonary oedema, sudden atrial fibrillation, arterial embolic episodes, and heart failure which can occur at any stage of pregnancy. Medical management with digitalis, diuretics, anti-arrhythmic drugs,

Antithyroid drugs; iodides	Foetal goitre
Azathioprine; mercaptopurine	**Susceptibility** to virus infection
Barbiturates (large doses)	Newborn withdrawal syndrome
Chloroquine	Retinal damage; multiple abnormalities
Coumarin anticoagulants	**Foetal haemorrhage; rarely, foetal abnormalities**
Diazepam and related benzodiazepines (large doses	Newborn withdrawal syndrome
Frusemide	**Maternal intravascular dehydration** and reduced placental perfusion leading to foetal growth retardation
Ganglion blockers	Paralytic ileus
Glucocorticoids	**Susceptibility** to virus infection; very rarely cleft palate
Live vaccines	Foetal virus infection
Narcotics	**Respiratory depression**; newborn withdrawal syndrome
19-Nor-steroids	Virilization of female fetus (transient clitoral hypertrophy; rarely labial fusion)
Phenytoi, primidone	Foetal abnormalities, foetal bleeding; newborn withdrawal syndrome
Rauwolfia alkaloids	Newborn depression syndrome
Streptomycin, kanamycin, gentamicin, vancomycin	**Sometimes minor 8th nerve damage** detected on audiometry, very rarely deafness
Vitamin D (large doses); dihydrotachysterol	**Skeletal abnormalities**

TABLE I.-Some therapeutic agents believed to convey a teratogenic risk in a small proportion of cases (From Hawkins, 1976; reproduced with permission)

Alcohol	Intrauterine and infant growth retardation; foetal abnormalities
Amine oxidase inhibitors	Foetal abnormalities; perinatal death
Amphetamines	Foetal thrombocytopenia
Antacids in first trimester	
Antiemetics, cyclizine	
Aspirin; phenacetin	Foetal abnormalities; foetal bleeding
Barbiturates in ordinary doses	Foetal abnormalities; minor skin malformations
Cannabis smoking	
Chlorpromazine (large doses)	Retinal damage
Chlorthiazide	Foetal thrombocytopenia
Idoxuridine	
Iron preparations in first trimester	
Lithium carbonate	
Lysergic acid diethylamide	
Meprobamate in first trimester	
Metronidazole	
Methyldopa (large doses)	Meconium ileus
Oral contraceptives	Limb and gastrointestinal abnormalities; neonatal jaundice
Oral pregnancy tests	Limb and other abnormalities, particularly in male foetuses
Oral hypoglycaemic agents	Foetal abnormalities; foetal hypoglycaemia and hypothyroidism
Podophyllin	
Propranolol	Intrauterine growth retardation
Quinine	Foetal abnormalities; foetal thrombocytopenia; middle ear damage
Stilboestrol	Vaginal adenosis and adenocarcinoma
Sulphonamides	Foetal abnormalities; neonatal jaundice
Tobacco smoking	Prematurity, intrauterine growth retardation; increased perinatal mortality
Tricyclic antidepressants	Foetal abnormalities; perinatal death
X-ray exposure	Foetal abnormalities; infant leukaemia and malignant disease

TABLE II. — Some drugs on which suspicion has been cast
Where no risk is indicated, an association with an overall increase in foetal abnormality has been suspected (From Hawkins, 1976; reproduced with permission)

antibiotics, anticoagulants (heparin, rather than warfarin is when feasible the anticoagulant of choice) and rest will be effective in most patients. However, closed mitral valvotomy or valve replacement may be necessary and, although the operative maternal risks are not appreciably greater, any surgical procedure does put two lives at risk. Therefore when possible elective surgery should take place before pregnancy or after delivery. Valve replacement is not in itself a contraindication to pregnancy, but special consideration has to be given to anticoagulant therapy and to the prevention of infective endocarditis.

Congenital heart disease

With the decline in the incidence of rheumatic heart disease, and the improvement of diagnostic assessment and corrective surgery for congenital heart defects, it is not surprising that congenital heart disease is being seen more frequently in pregnancy. Pregnancy can be managed successfully in most forms of congenital heart disease, but the maternal and foetal mortality is high in patients with Eisenmenger's syndrome although, with diligent supervision, pregnancy may be safely concluded even when this condition is present (Condrasson and Werkö, 1974). All patients with congential heart disease will need careful supervision throughout pregnancy and the puerperium.

Ischaemic heart disease

The incidence of ischaemic heart disease in women is increasing and consequently more women with this condition are becoming pregnant. Management does not differ basically from the non-pregnant state and, if careful supervision is given, pregnancy can be brought successfully to term. Coronary artery bypass surgery is not in itself a contradiction to pregnancy.

Anaemia

The expansion of the plasma volume in pregnancy causes haemodilution with a fall in the haemoglobin concentration from pre-pregnancy levels of 14g/dl to levels around 11g/dl in late pregnancy — 'the physiological anaemia of pregnancy' — and, although the wisdom of administering iron has been debated, studies do show that iron supplementation improves the oxygen carrying capacity of maternal blood during pregnancy (Metcalfe and Ueland, 1974). At present it would probably be premature to withdraw routine prophylactic treatment with combined iron and folate supplements (Scott *et al.*, 1975), although there is no evidence that prophylaxis with either is necessary in developed countries (Hall, 1974).

With the increasing immigrant population in Britain the incidence of haemoglobinopathies in pregnancy, most noticeably sickle-cell anaemia and β-thalassaemia major, has increased (Huntsman, 1976). Patients with sickle-cell disease may develop infarctive crises presenting with joint or bone pain, generalized abdominal pain, pulmonary infarction and cerebral embolism which may cause transient or permanent neurological manifestations, and the incidence of eclampsia is increased. An aplastic crisis can occur with marrow output failure and the haemoglobin level may fall suddenly in an acute sequestration or haemolytic crisis. As maternal mortality and foetal loss are increased, good obstetric management is essential. The sickle-cell trait carrier does not appear to have a higher maternal risk or neonatal mortality but anaesthetic procedures may be hazardous (Huntsman, 1976). Genetic counselling will be an important aspect to management in most haemoglobinopathies.

Urinary tract infections

Bacteriuria may be found in 5 to 8% of pregnant women depending on age, parity or social class (Davies, 1976), but the relationship between these factors and low birth weight and increased perinatal mortality is a complex and controversial topic. There is little doubt that urinary and genital tract infections in the mother may have serious consequences for the foetus, particularly if the defence mechanisms are altered, for example by pre-term delivery (Reid, 1975; Davies, 1976). To date the importance of this association is not clear and policy is tempered by the difficulty on the one hand of diagnosing maternal infection, and on the other by reluctance to encourage the indiscriminate use of antibiotic pro-

phylaxis. Women with symptoms of a urinary or genital-tract infection, those at risk because of previous renal disease or a history of urinary-tract infection, should have bacteriological studies and careful follow-up throughout pregnancy with consideration being given to the timing of delivery.

Drugs and smoking in pregnancy

The reader is referred to the detailed and sensible review of Hawkins (1976) which concludes; 'the practitioner who restricts his prescribing for pregnant women to circumstances where medication is really indicated, and employs medicines which have been widely used in pregnancy for many years without apparent harm is unlikely to contribute significantly to the incidence of congenital malformation'.

Some drugs, such as thalidomide, the antitimetabolites and antimitotic drugs are major teratogens and should not be used in pregnancy, and tetracycline which discolours and causes enamel hypoplasia of deciduous teeth should be avoided. There are a number of therapeutic agents which may convey a small risk to the foetus (table I), and a decision to use these drugs must be carefully balanced by considering the risks of the maternal condition requiring treatment and the danger to the exposed foetus. A compromise of careful management and minimal drug exposure is usually possible. There are a number of drugs (table II) which are regarded with suspicion in pregnancy but as yet there is no established proof.

A few practical points can be made. The number of cases of foetal abnormality associated with oral contraceptives is small, and the case is as yet unproven. There can be no justification for the administration of hormones in early pregnancy in the form of 'oral pregnancy tests', nor do the 19-nor-steroids have any value in pregnancy maintenance and their use should be abandoned (Hawkins, 1976).

Pregnant women on phenytoin for epilepsy should take folic acid supplements throughout, and vitamin K should be given to mothers early in labour. Babies born to mothers taking barbiturates for epilepsy or other reasons, will have to be observed for signs of a sedative withdrawal syndrome, and a number of problems may occur in the newborn of alcoholic mothers.

Although the case against smoking in pregnancy is still being debated (Hawkins 1976), small-for-dates babies, premature labour and possibly increased perinatal mortality have been attributed to smoking and, because of this and the potential benefit to maternal health, all pregnant mothers should be encouraged to moderate, if not cease, cigarette smoking altogether.

The recommendation of the Royal College of Radiologists that all but urgent radiological examination should take place during the second half of the menstrual cycle to avoid risk to an early conceptus is obviously reasonable, and every effort to reduce exposure of the foetus to radiation at any stage of pregnancy is desirable. (Hawkins, 1976).

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