Cystic fibrosis and pregnancy

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Increasing numbers of women with cystic fibrosis (CF) are now reaching child-bearing age. Many wish to have families and hundreds have already done so, usually successfully. While there are a large number of important issues involved in pregnancy for a CF mother and particular care must be taken in medical management at this time, in general the outcome is good and CF women in reasonable health who wish to have a family can be encouraged to do so. Medical and obstetric advice and management need to be coordinated and this is best done in a specialist CF unit.

Fertility, contraception and family planning

It is often stated that CF women are less fertile than normal although there is little supporting data[1]. Certainly severe episodes of infection together with malnutrition both lead to menstrual irregularity and so fertility is likely to be impaired in those with advanced CF lung disease. In contrast, those with mild disease usually conceive without great difficulty, in spite of the theoretical problems of dehydrated cervical mucus perhaps leading to impaired sperm penetration.

Issues of contraception are therefore broadly similar for CF and non CF women, although there are a few important differences. In the first place an unwanted pregnancy should be strenuously avoided in CF both because a therapeutic abortion is particularly undesirable in a woman with chest problems and also because the additional demands of a child without good family support are especially difficult for a CF mother. Secondly, oral contraceptives may be slightly less reliable in CF because of unpredictable absorption from the gut and so very low dose preparations are best avoided, while high oestrogen preparations carry a slight risk of thrombosis or liver damage.

When a pregnancy is being planned the important considerations are timing, family support and genetics of the father. The ideal time for a CF mother to have children is relatively early when her own health problems are mild. Even though many people with CF now remain well into their 30s and 40s this cannot be relied upon and naturally a mother will look after her child better if her own health is good. Family support is particularly important since a CF mother can expect at best some episodes of ill health when she may need to be in hospital during the child's first few years. At worst the mother may become severely or even terminally ill.

The risk of the child having CF is about one in 50 (the father has a 1 in 25 chance of being a carrier). Carrier testing of the father reduces this risk considerably if he does not carry one of the common CF mutations. If however the father is found to be a carrier the risk is then very high (1 in 2) and the couple may decide not to proceed.

Physiological consequences of pregnancy

The effects of pregnancy on lung function in women with and without lung disease have been well reviewed[2] and the changes in lung volumes, respiratory drive and blood volume will only be summarized here. Lung volumes are reduced by the growing uterus as it pushes up the diaphragm and so total lung capacity, vital capacity and tidal volume fall in healthy women. In CF these lung volumes are limited more by the state of the airways than the size of the thoracic cage and so pregnancy may make little difference. Nevertheless, any additional reduction can be very important. Surprisingly, some reports of CF mothers have shown the opposite changes but these are likely to be exceptions[3].

Respiratory drive increases during pregnancy and minute ventilation rises. This is in part due to the action of progestogens on the respiratory centre and in part to the increased metabolic rate. As a result the PaO_2 rises slightly and the $PaCO_2$ falls. Mild breathlessness is noticed by women with normal lungs and this is worse if lung function is impaired. In the extreme case (when pregnancy is highly undesirable), minute ventilation cannot increase enough and so the $PaCO_2$ rises. The blood volume and cardiac output rise by as much as 50% towards the end of pregnancy as a result of the new placental circulation as well as general vasodilation. These changes can precipitate cor pulmonale in the presence of severe lung disease.

The nutritional consequences of pregnancy can be particularly important in CF. Normally there is a 5-10 kg weight gain as the mother has to eat enough for herself as well as the developing baby both during pregnancy and lactation. In CF when nutrition is often suboptimal before pregnancy this extra can be very difficult to achieve.

Pregnancy in CF

In spite of the above difficulties the experience has, in general, been good. The largest review by Cohen in 1980[4] gave details of 129 pregnancies in 100 women. The results are summarized in Figure 1. Twenty-six of the pregnancies were completed preterm (<37 weeks) and 10 of the 11 perinatal deaths occurred in this group.

The mothers' health was also reported although details were less complete. There were no deaths during pregnancy but 15 (18%) died within 2 years of delivery. This mortality rate was the same as that expected for non pregnant CF women of the same age. All of the women who died had moderately severe or severe lung disease before pregnancy and both

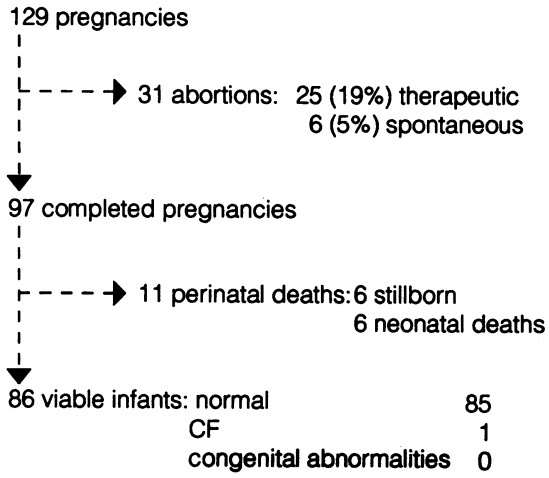

Figure 1.

perinatal death and pre-term delivery were associated with these maternal deaths. Heart failure developed in nine women and maternal weight gain was less than 4.5 kg in 34. Other complications were hypoglycaemia, vaginal haemorrhage, renal failure, pre-eclampsia, hypoprothrombinaemia and placental abruption (one patient each).

Statistical analysis of these results was impeded by patchy data but maternal breathlessness and cyanosis were associated with maternal mortality, and poor maternal weight gain predicted prematurity and still birth. In summary, it is clear that for most pregnancies the outcome for both mother and child was good while poor respiratory health pre-pregnancy predicted a poor outcome.

No precise values of lung function or weight can be given below which the outcome will be bad, but an FEV_1 or FVC of less than 60% and weight of less than 85% predicted are a reasonable guide[5]. Similarly, a raised $PaCO_2$, a SaO_2 of $<90\%$ and cor pulmonale all indicate a dangerous level of lung damage. A Shwachman score of over 80 has been proposed[4] as desirable for a prospective mother.

Medical management during pregnancy

This follows conventional lines with extra emphasis on the control of pulmonary infection and adequate nutrition. The risks to the fetus from poor maternal health is probably greater than the risk of drugs crossing the placenta and full courses of antibiotics should be given. Regular routine admission for rest and chest treatment during the pregnancy and before delivery may be needed for those with moderate or severe lung disease.

Dietary advice and nutritional supplements are routine and occasionally intravenous nutrition for short periods may be needed, eg for severe first trimester vomiting.

A full-term normal delivery is usually achieved and nutritional supplements may need to be continued to supply the additional demands of breast feeding. Breast milk is normal in CF although some drugs given to the mother may be secreted.

Maternal drugs and the fetus

The experience has so far been good and congenital anomalies have not been a problem with CF pregnancies. Nevertheless, the fetus will often be at risk from maternal drugs and from relative hypoxia. The guiding principles at present are: first to avoid drugs with a record of teratogenicity, second to avoid as far as possible new drugs with an unproven record and third to ensure optimal maternal nutrition and lung health. Problems can arise when the only effective antibiotic is new and has an unproven record of use in pregnancy. In this situation the risk of poor maternal health is probably the greater and the drug should be given. The drugs used to prevent rejection following lung transplantation are potentially teratogenic and pregnancy should not occur in this situation.

The future

More and more CF pregnancies can be expected and encouraged. With sensible family planning, avoidance of pregnancy in those with severe disease and good medical supervision before, during and after the pregnancy the outcome for both mother and child should continue to be good. Experience of CF pregnancies can best be gained in a specialist CF unit and outcome is likely to be better for patients managed in this way.

References

1 Oppenheimer EH, Case AL, Esterly JR. Cervical mucus in cystic fibrosis: a possible cause of infertility. *Am J Obstet Gynecol* 1970;**108**:673-4
2 Weinberger WE, Weiss SJ, Cohen WR, *et al.* Pregnancy and the lung. *Am Rev Respir Dis* 1980;**121**:559-81
3 Novy MJ, Tyler JM, Shwachman H, *et al.* Cystic fibrosis and pregnancy: report of a case, with study of pulmonary function and arterial blood gases. *Obstet Gynecol* 1967; **30**:530-6
4 Cohen LF, Di'Saint'Agnese PA, Friedlander J. Cystic fibrosis and pregnancy. *Lancet* 1980;**ii**:842-4
5 Palmer J, Dilloon-Baker C, Tecklin JS, *et al.* Pregnancy in patients with cystic fibrosis. *Ann Intern Med* 1983; **99**:596-600