cluded in the survey must be a high proportion of the total treated in Britain in that period. The results are very similar to those in the European and international transplant series from the same era. After renal transplantation some 60% of patients and 40% of grafts survived for three years. Patients treated by haemodialysis alone had a better chance of survival—a conclusion which may also be drawn from European and predominantly American statistics, though with the caution necessary in retrospective analysis of unmatched groups.

The implications of these findings have been analysed by a team of doctors and computer scientists at the London Hospital, and their forecasts for the next five years are given in an article at p. 686. Dr. S. C. Farrow and his colleagues calculate that if units continue to accept patients at the present rate then by 1976 there would be about 1,700 patients on dialysis, mostly at home, and about 500 patients on functioning grafts. An increase in the intake of patients to the maximum possible rate and a reduction in the average waiting time for a transplant from two years to one could raise these figures to 4,000 and 1,000 respectively. But, say the London Hospital team, this considerable increase in the number of transplant operations would lead to only a relatively small increase in the number of patients alive with functioning transplants in 1976: since many would have died and others would have returned to dialysis. It could be argued, they say, that it would be better to rely on dialysis alone for the time being and to step up the rate of transplant operations only when patient and graft survival have improved with the advances that seem bound to come.

Such a view would seem unduly pessimistic. The Joint Committee report points out that whereas survival rates from dialysis seem unlikely to improve those from transplantation are getting steadily better, and it also stresses that the life of a patient with a functioning transplant is much more pleasant than that on dialysis. Even a 60% survival in a uniformly fatal disease is a great encouragement to those who work in the field and who daily encounter the patients who have achieved full social, sexual, occupational, and emotional rehabilitation, but it may fall short of the convincing demonstration that is needed to overcome the fears of the rest of the medical profession. If so this is unfortunate: for it is doctors outside the renal units who need to be convinced if more kidneys are to be made available. Shortage of cadaver kidneys compels the transplant team to accept poorer tissue matches than it would wish, and this prevents the improvement in long-term results which is needed to convert the waverers. Probably we have been aiming too low in tissue matching. The Joint Committee report shows that women fare worse than men after transplantation, and this probably reflects their higher incidence of cytotoxic antibodies after pregnancy. Such antibodies are not always easy to detect, and they imperil renal transplants even in the presence of a negative cross-match unless tissue matching is extremely close. Ideally every patient should be offered a “full house” match, but if we are to approach this ideal many more kidneys must be offered than are actually used. This requires a great deal of sympathy and altruism from colleagues who stand to gain nothing for their own patients in return.

2 Kerr, D. N. S., Proceedings of the Royal Society of Medicine, 1967, 60, 1195.

Physiology of the Fetus

A proper understanding of the physiology of the fetus is becoming an essential prerequisite in the training of obstetricians. It seems remarkable that such comment has to be made when adult physiology has been taught to medical students for so many years. It is even more remarkable that an acceptable standard of obstetric care has been provided for so many years when most doctors have only a few hazy concepts of how the fetus develops and responds to the stress of labour. There are several explanations for this apparent disregard of fetal physiology: the difficulty of studying even the animal fetus under physiological conditions; a deep distrust by clinicians of the relevance of animal studies to human problems; and the overriding need to ensure that pregnancy is safe for the mother. Nevertheless, it is still difficult to understand the failure of many obstetricians to recognize that though in most women pregnancy is a physiological event resulting in a healthy baby, in a few the environment of the fetus may become so adverse that future development may be permanently impaired.

A recent symposium on fetal physiology held in Cambridge to mark the centenary of Sir Joseph Barcroft’s birth was attended by physiologists from all over the world including many friends and colleagues who knew him when he was professor of physiology at the university there. To Sir Joseph must go the major credit for laying the foundations of modern research into fetal life. Probably his interest in the fetus, which came late in life, originated from his interest in the greater affinity of fetal haemoglobin for oxygen to which he ascribed the ability of the fetus to develop normally. Once involved, Barcroft spent the major part of the latter years of his life studying all aspects of fetal life culminating in the publication in 1946 of his classic book Researches on Prenatal Life. Reading through this today one cannot be but impressed by the fact that most of his observations have been validated by subsequent work.

It is unlikely that many of Barcroft students realized the relevance of his work to clinical obstetrics, and most likely they dismissed its practical importance. Work reported at the Cambridge symposium showed that attitudes have changed remarkably and many obstetricians are now undertaking fetal physiological research. Much of the credit for the spread of knowledge must go to Barcroft’s successors such as D. S. Barron in the U.S.A. and G. S. Dawer in Britain, who for many years have taken young clinicians into their laboratories for a period of physiological research.

The field of fetal physiology is so wide that it was with
some difficulty that 67 papers on a variety of topics were fitted into the three days of the Cambridge symposium. So high was the standard of the papers that it would be invidious to select any of particular merit. Nevertheless, the work of G. C. Liggins, an obstetrician from Auckland in New Zealand, does deserve special mention because it exemplifies the potential value to clinical medicine of basic biological research. While studying the factors responsible for parturition in sheep he noted that in the immature lamb respiratory function after birth was improved by the infusion of glucocorticoids during fetal life. A subsequent trial amongst women going into premature labour has now shown that there is a significantly lower incidence of respiratory distress and mortality among the babies of mothers treated with betamethasone. This appears to be due to the induction of surfactant formation in fetal lungs. Though the mechanism is not fully understood, clearly the observation is important, implying that it may eventually be possible to diminish the incidence of the major cause of perinatal mortality.

There can be little doubt that if Sir Joseph were alive today he would be delighted by the flowering of the seed he planted. The present symposium was held 25 years after his death, but it is certain that the interval before the next symposium will need to be much less if we are to keep pace with the present rate of progress in fetal physiology.

**Unusual Symptoms of Crohn’s Disease**

Patients with Crohn’s disease nearly always present with symptoms due to the intestinal lesions—diarrhoea and abdominal pain—and often a tender mass is palpable in the right iliac fossa or the hypogastrium. There may be an accompanying high pyrexia, loss of weight, and iron-deficiency anaemia. Crohn’s disease may also be accompanied by general symptoms much like those seen in ulcerative colitis. These include polyarthritis, ankylosing spondylitis, iridocyclitis, erythema nodosum, and finger clubbing. Clubbing, for example, was noted in 105 of 181 patients with Crohn’s disease studied by J. P. Fielding and W. T. Cooke, and it was found to be related to the activity but not to the site of the disease. The clubbing would disappear two to three months after the disease became quiescent.

Perianal disease, taking the form of deep multiple fissures, undermining anal ulceration, indolent fistula-in-ano, or oedematous skin tags, is now known to be common. It is especially likely to complicate Crohn’s disease affecting the large bowel, but it may also complicate Crohn’s disease otherwise confined to the small intestine. It is important to note that an anal lesion may precede the onset of intestinal symptoms, and this occurred in one-quarter of the cases studied at St. Mark’s Hospital by W. N. W. Baker and G. J. Milton-Thompson. J. C. Mountain has recently described three examples of metastatic ulceration (affecting the base of the penis, the submammary region, and the abdominal wall) complicating Crohn’s disease associated with perineal ulceration. These lesions gave the typical granulomatous picture of Crohn’s disease on histological examination.

In 1969 T. P. Dudeney reported a patient of 36 with Crohn’s disease of the ileum who developed an area of granulation tissue on his buccal mucosa, a biopsy of which showed plasma cell infiltration and one or two epithelioid and giant-cell foci. This appears to be the first example of Crohn’s disease affecting the mouth. K. F. R. Schiller and his colleagues described three patients with oral and one with labial Crohn’s disease, histologically confirmed. These presented with a hypertrophic oral mucosa, an indurated polypoid lesion, or a linear ulcer.

The most detailed study of this symptom of Crohn’s disease is that of C. B. Croft and A. R. Wilkinson, who have reviewed 512 cases treated at the Leeds General Infirmary. Twenty patients (61%) were found to have suffered from oral ulceration at some stage during their illness. In three the oral ulceration was a presenting feature of the illness, and in one the onset preceded bowel symptoms by one month. One of the patients was of particular interest in that he showed severe ulceration of the mouth and pharyngeal mucosa with ulceration and oedema of the epiglottis and larynx. Histological studies were compatible with a diagnosis of Crohn’s disease, and this appears to be the first example of lesions of the laryngopharynx in a patient with Crohn’s disease of the intestine. Evidently clinicians should be aware of this possible symptom of Crohn’s disease, especially as it may mimic oral candidiasis or vitamin deficiency, both of which may complicate severe Crohn’s disease.


**Better Influenza Vaccines?**

No one is particularly satisfied with the present influenza virus vaccines, and there are several reasons for this. They have to be given annually, because immunity declines in a matter of months, and though the decline can be overcome by using oil adjuvants these occasionally produce local lesions of unacceptable severity. Adjuvants made with oils that can be metabolized may yet prove satisfactory.

Another problem is that suitable vaccines are always scarce when an epidemic due to a new type of virus comes along. The reason is that the virus spreads round the world before manufacturers can produce the vaccine. But recently they have been exploiting techniques developed for what seemed at the time an unusually esoteric branch of science —namely, influenza virus genetics. The technique is recombination of genetic material. By its means one can introduce in a few days into a new strain, with new antigens on its surface, the capacity to grow freely and rapidly in eggs, which is otherwise acquired only rather unpredictably and by tedious serial passage in the laboratory. The idea was put forward years ago by E. D. Kilbourne in the U.S.A., and vaccines recently made in Britain by this technique have proved satisfactory, as have similar experimental vaccines in the U.S.A.

Live influenza vaccines might solve some other problems, for they can be given without injections and they require less virus per dose. In fact, if mass vaccination against influenza were ever to be practised, it would be almost essential to use live vaccine. Here again recombinants may be helpful, for it has been shown that the same method may