mation of the risk of Down's syndrome for each pregnancy. In a retrospective analysis a positive result would have occurred in 61% of pregnancies in which the fetus had Down's syndrome, with a false positive rate of 5%.² Prospective analyses have reported detection rates of 48% to 91%, with false positive rates of 3.7% to 5.7%.³⁻⁵ This non-invasive method of screening makes it possible for all pregnant women to be aware of their individual risk. Thus younger women who are positive on screening may decide to opt for amniocentesis or chorionic villus sampling, while older women who are negative are spared the risk of an invasive procedure.

In this week's journal Green presents the results of a postal survey of obstetricians' views of serum screening in England and Wales,⁶ and Smith and colleagues present the findings of a questionnaire completed by women after they had discussed biochemical screening with a midwife or obstetrician.⁷ Both papers make for uncomfortable reading. The survey of obstetricians reports that biochemical screening for Down's syndrome was not universally available in July 1993. Interestingly, one in five respondents said that biochemical screening had been introduced in their units as the result of unspecified "outside pressures," while an equal number wanted to introduce biochemical screening but were prevented from doing so by outside pressures. Where biochemical screening had been introduced, difficulties had been encountered in providing adequate counselling before and after the test.

Green rightly draws attention to the trend towards community based antenatal care and raises the question of who will provide the counselling, ensure satisfactory standards, and, most importantly, bear the cost. Furthermore, women who are positive on screening are more likely to opt for amniocentesis or chorionic villus sampling than previously. Provision will have to be made for the costs of laboratory investigation and counselling associated with these procedures.

Adequate counselling before the test should help women to decide whether to opt for biochemical screening, allevi-

ate much of the anxiety associated with a false positive result, and raise appreciation of the possibility of a false negative result.

Smith and colleagues' report shows the poor knowledge that many women have about the implications of false positive and false negative results—even after an obstetric consultation. This must partly reflect the confusion within the profession, as highlighted by Green. The Royal College of Obstetricians and Gynaecologists has defined the essential components of best practice,⁸ and further work is required to investigate whether these are being provided, and if not, the reasons for this.

Alternatives to biochemical screening are being reported,⁹ and some form of screening for Down's syndrome will probably become available for most pregnant women in the future. Although the methods of screening may vary, the requirement for clear, unbiased, knowledgeable advice will be common to them all. Resources will have to be allocated for population counselling as well as screening if we are to do more good than harm.

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Insulin dependent diabetes mellitus: a lethal disease in the developing world

Some patients are dying for lack of insulin

Before the discovery of insulin in 1921 the diagnosis of insulin dependent diabetes mellitus was tantamount to a death sentence, with 40% or more diabetic patients dying of ketoacidosis. This changed dramatically after 1921, with ketoacidosis becoming a minor cause of death. Life expectancy increased appreciably, although not to the extent hoped for because of the emergence of nephropathy and ischaemic heart disease.

Now, with improved treatment and prevention, life expectancy is good for a patient with newly diagnosed insulin dependent diabetes mellitus. Thus someone in whom the disease was diagnosed before the age of 17 in Pittsburgh between 1950 and 1981 had an 88% chance of surviving 20 years.¹ Survival now would be even better, and the results of the recent diabetic control and complications trial give hope for further improvement.²

Sadly, this is not the situation worldwide. Insulin depen-

dent diabetes mellitus is not only a disorder of developed countries: it occurs everywhere, although its incidence varies widely from about 2-4 per 100 000 in parts of sub-Saharan Africa³ to 14 per 100 000 in Britain. A substantial number of children are affected, and in some developing countries, such as Sudan, rates are close to those in Britain.⁴

Life expectancy in developing countries is substantially less than that in developed countries, although reliable data are few. In Tanzania mortality of patients with insulin dependent diabetes was found to be 40% after a mean of five years.⁵ The main causes of death in those dying in hospital were ketoacidosis (50%) and infection (32%)—mirroring the patterns observed in Europe and the United States in the preinsulin era.⁶ Deaths outside hospital were probably due to ketoacidosis and hypoglycaemia. Many reasons exist for this high mortality, but the main one is the

inconsistent and erratic supply of insulin. Because insulin dependence in diabetes implies lifelong dependence, a regular and consistent supply of insulin is needed. The International Diabetes Federation has always advocated that insulin should be freely available to all those who need it, while a recently published report from a World Health Organisation study group states: "In all countries, the availability of insulin as an essential life-saving drug should be ensured, without imposition of taxes or restrictions regarding the transfer of technology for its manufacture."⁷

Problems with the supply of insulin in the developing world have been reported anecdotally for many years. Recently three reports have highlighted the problem. In one McLarty *et al* distributed a questionnaire in Africa through two journals⁸; Savage did the same through Equipment Charity Hospitals Overseas (ECHO).⁹ In the third, the International Diabetes Federation sent a questionnaire to its 105 member associations in 85 countries.¹⁰ All came to the same conclusions: that in many countries insulin supplies were erratic and often not available to people with insulin dependent diabetes mellitus. McLarty *et al* received replies from 50 practitioners working in 25 African countries. Most commented that insulin was rarely available in rural areas. Only 36% believed that insulin was available sometimes in small towns, and half reported that insulin was sometimes unavailable in large urban centres. Even when it was available in some cities most patients could not afford it. Insulin was unavailable for at least some of the time in 22% of countries and was free in only two thirds of the countries.

The costs of insulin varied widely around the world; one phial cost from \$2.70 to \$22 (£1.80 to £15). The cheapest supplies were not necessarily available in the poorest countries. In Tanzania, for example, where patients may need to buy insulin, it can cost \$15 (£10) per phial-equivalent to one month's pay for many people. To this must be added the cost of syringes and monitoring materials, which are often not available. Colleagues and I have calculated that the annual cost of insulin alone for sub-Saharan Africa, excluding South Africa, is roughly \$25m (£16m), on the basis of Tanzanian estimates of \$156 (£104) per patient.⁸

Diabetes tends to be ignored in the face of major disasters such as famine, drought, and genocide, but people with insulin dependent diabetes mellitus have a right to life; and at a relatively small cost per patient by Western standards many more could have a productive life—and, indeed, could live.

The situation has been worsened by the policies of the International Monetary Fund and World Bank, which are attempting to ensure that health care systems stay within their very limited budget and that patients contribute to costs of care. This is clearly impossible for people with diabetes in the poorest countries. Some countries—for example, Bangladesh—are strikingly successful in ensuring that insulin is available for all, but this is the exception.

In parallel, an unofficial group working out of Melbourne under the umbrella of the International Diabetes Federation has been instrumental in providing insulin for emergency use in several countries, particularly in Africa; but should we have to rely on charitable donations for such a fundamental drug? Industry could help by charging less for insulin in the poorest countries, but it fears that this would lead to re-export to Western countries and large mark ups by unscrupulous middle men. Recently a man was arrested at Cairo airport attempting to smuggle out 500 000 doses of insulin, purchased at a highly subsidised price, to resell abroad.¹¹ In the end it is the responsibility of governments to ensure that drugs such as insulin are available for those who need them. And it is up to the diabetic community and health care professionals to ensure that this comes about.

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Understanding clinical trials

What measures of efficacy should journal articles provide busy clinicians?

See article on page 761

The randomised clinical trial has revolutionised the way that we decide whether a treatment or intervention does more good than harm. In its breadth and explanatory power it provides a cornerstone not only for evidence based medicine¹ but for evidence based public health, evidence based hospital administration, evidence based purchasing, and evidence based consumerism.

Randomised trials provide not only qualitative conclusions about whether a treatment is better but also quantitative estimates of the extent to which it is better. Take as an example (with rounded numbers) an overview of the

effects of treatment with antihypertensive drugs on patients with moderate to severe hypertension. Trials have shown that about 1800 strokes occur among 15 000 patients randomised to active drugs for an average of five years, while about 3000 such events occur in 15 000 randomised to placebo or no active treatment.² This difference in stroke is extremely unlikely to be due to chance (in other words it is highly significant statistically), providing the qualitative answer that antihypertensive drugs are better than no treatment for patients with moderate to severe hypertension.