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The flow cytometer

The flow cytometer is one of the most exciting of recent innovations in pathology.^{1,2} It produces measurements on thousands of cells that are forced one by one at high speed through a focused light beam (usually produced by a laser). Some of the information that would be available from a microscope can be gathered in this way, but, in addition, the cytometer assigns accurate quantitative values to the information, computes the inter-relationships between the measurements, and may then sort out from the original samples cells with particular characteristics. One possibility is thus that cervical screening might be automated, but the technology is not yet good enough.

The cytometer measures simultaneously the forward and lateral light scatter (proportional to cell size and cytoplasmic optical "texture" respectively) and the intensity of any fluorescence deriving from DNA or protein seeking fluorescent tracers to which the cells have been exposed. Such tracers include DNA binding dyes (for nuclear DNA content) and a potentially limitless range of antibodies to cellular constituents, tagged with fluorochromes. Suitable fluorochromes are fluorescein and phycoerythrin, which emit at different wavelengths and so allow simultaneous double labelling.

Flow cytometers require the cells to be in an evenly dispersed suspension. Blood cells come this way naturally, and cytology specimens and lymphoid tissues can be rendered suitable by gentle physical means. Solid tissues must be digested enzymically. Thus the flow cytometer does not give any of the information on cell to cell orientation which is so important in histopathology.

Early research applications of flow cytometry were in immunology, and modest instruments can provide good immunophenotypes from peripheral blood leucocytes. In the study of tumours applications include estimating the proportion of cells engaged in DNA synthesis and the proportion sensitive to radiation—both useful indices in monitoring treatment. Most useful, however, is the ability to measure the basal DNA content of tumour cells. The degree of DNA aneuploidy is related to the prognosis of tumours at many sites, including ovary and bladder—where histological examination is sometimes an uncertain guide to the aggressiveness of the tumour. DNA content can be measured in nuclei recovered from thick sections of specimens processed in paraffin,³ which means that the power of this new technology

can be evaluated using stored blocks of tissues from patients whose ultimate clinical progress is already known. We will soon be reading many reports of studies on archival material.

The flow cytometer cannot be used for cervical screening, partly because of inadequate sensitivity. Whereas a good cytologist will be alerted by two or three abnormal cells in a smear of around 15 000 cells, the cytometer would barely detect 10 times that proportion.⁴ Another problem is what to measure: DNA aneuploidy, although correlating with the grade of cervical intraepithelial neoplasia,⁵ is not a satisfactory criterion on its own. Better discrimination may be provided by simultaneous analysis of other values, and there are reasons for optimism as more antibodies to tumour markers become available, including some to oncogene proteins that are presumably close to the origins of the neoplastic process itself. An instrument operable by a skilled technician and able to discriminate between normal and atypical smears without error or fatigue would bring solace today not only to the women waiting for smear results but also to doctors, cytologists, and health board administrators—even if it costs (as good ones do) over £150 000.

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The economics of mental health services

The most cost effective way to deliver mental health care is not clear.¹⁻⁴ In the move from hospital to community care the patterns of use and financing of mental health services are changing rapidly—as are the distribution and responsibilities of staff. And developing optimal services is difficult because of the lack of reliable measures of process and outcome and of the costs and benefits of identification and treatment.

In fact, different types of hospital care result in similar clinical and social outcomes. In one study newly admitted patients were randomly assigned to standard inpatient care followed by outpatient care, brief admission followed by discharge to outpatient care, or brief admission followed by day care and then discharge to outpatient care.⁵ Brief admission followed by either day or outpatient care was less expensive after two years than standard admission both in hospital costs and in costs to the patients' families. In a similar study patients admitted as emergencies with neurosis, personality disorder, or adjustment reaction were randomly allocated to day hospital or inpatient care.⁶ After one year the median length of stay for day care was twice as

long as for inpatient care. Despite this the average cost of day care was about two thirds the cost of the cheaper of the two inpatient regimens. A third investigation looked at two cohorts of patients who had had a first admission for schizophrenia four years earlier.⁷ One cohort was treated in a teaching district general hospital and the other in an area mental hospital. Those treated in the district general hospital had significantly shorter stays and so the total hospital costs were less than those for the area mental hospital despite higher unit costs. According to a recent report, this empirical economic superiority of district general hospitals generalises to everyday service provision.⁸

By contrast, several randomised controlled studies show that care provided around the clock, seven days a week in the community has clinical, social, and economic advantages over hospital care. For example, comprehensive community care for patients presenting for admission was considered significantly more satisfactory by patients and their relatives, did not increase the burden on the community, and cost less than standard hospital care and aftercare.⁹ An assertive, intensive, and supportive programme of community treatment for chronically disabled patients was found to be cheaper than mental hospital treatment and showed additional non-monetary advantages.¹⁰ Treatment at home was less expensive over one year than hospital care for patients destined for admission,¹¹ and, finally, family management at home for patients with schizophrenia was more than twice as cost efficient as clinic based care.¹²

Two trials have shown clinical and economic benefits from nurses treating patients with neurotic disorders in the community.^{13 14} Data from the Salford case register show, however, that community psychiatric nurses are treating patients found in primary care rather than reducing the demands made on traditional services.¹⁵

Taken at face value the evidence suggests that services relying wholly or mainly on treatment in the community tend to be more cost effective and to be preferred by consumers. But most investigations fail to acknowledge the large part played by general practitioners in treating people with psychiatric morbidity who come to medical attention, only about 5% of whom are referred to specialist services.¹⁶ There are two main consequences. Firstly, studies of local mental health services should include data on general practice; statutory, voluntary, and self help agencies¹⁷; and the private sector.¹⁸ Secondly, the most efficient functions for individual mental health service providers must be found—inevitably this raises issues of manpower and remuneration. One question immediately arises: should more than only one in five psychiatrists spend time in general practice?¹⁹

Scope exists for making savings through improved efficiency, but additional expenditure is also needed to start new services. Ironically, data collection for health services research is also threatened by cuts: "The end result could be that there was no information available on which any kind of rational decision could be based. The temptation to draw the cynical conclusion—that this is precisely the situation which many governments would like—ought, presumably, to be resisted.... As resources dwindle information becomes more, not less, important."²⁰

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Reversal of female sterilisation

Every patient who requests sterilisation is told that the effect of the operation is permanent, but most patients know that this is not always true—and requests for reversal are increasing.

Dissatisfaction with temporary methods of contraception and the safety and simplicity of laparoscopic sterilisation have led in the past 15 years to a large increase in women asking for sterilisation. If the 1985 Welsh figures of 6030 sterilisations (Welsh Office, personal communication) are multiplied up they suggest about 100 000 such operations each year in England and Wales. This total has changed little in the past three years, and worldwide over 60 million women have been sterilised.² About 10% of women express some regret after sterilisation, and between 0.1%² and 5%³ ask for reversal. Among those considered suitable for operation the chances of successful pregnancy have increased from 22% in 1975⁴ to over 80%^{2 5-7} in some circumstances today, although the rate of ectopic pregnancy after the operation remains about 3%.⁷

The patients most likely to request reversal are those sterilised below the age of 30, those with an unstable marriage, and those from lower socioeconomic groups. They have often been sterilised immediately after a pregnancy, show more neurotic traits, and have had more contraceptive problems than those sterilised at an older age with no regrets.⁸⁻¹¹ Two thirds of the women requesting reversal want children by a new partner—usually one younger than themselves.⁸

The increase in the success rate of reversal operations is caused as much by changes in the technique of sterilisation as