Clearview pregnancy test results. The horizontal bar in the top chamber shows that a urine sample has progressed satisfactorily from the lower chamber. A horizontal bar in the middle chamber shows a positive result (left) and its absence a negative result (right).

Enzyme linked immunosorbant assays (ELISAs) are the bases of many of the commercial kits currently available in chemist shops. The assay depends on the double reaction of standard phase antibody with enzyme labelled antibody, which is sensitive and so able to detect very low concentrations of human chorionic gonadotrophin. Positive results are therefore detectable as early as 10 days after fertilisation—that is, four days before the first missed period.

Conclusions

I thank Mr Malcolm Pearce of St George's Hospital Medical School for reading all the articles in this series, making helpful suggestions, and not objecting when I did not follow all of them. The picture of the infant welfare clinic is reproduced by permission of William Heinemann from *University College Hospital and its Medical School: a History* by W R Merrington.

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At the end of the preliminary consultation women may ask questions about the pregnancy, and the practitioner will deal with these. Most of these queries will be considered in a future article on normal antenatal management. For most women the onset of pregnancy is a desired and happy event, but for a few it may not be so and the practitioner, having established a diagnosis, may find that he is then asked to advise on termination of pregnancy. This he should do if his views on the subject allow; if not, he should arrange for one of his partners to discuss it with the woman. For most women, however, the pregnancy will continue to a much desired result.

Letter from Chicago

Voices of the moon

George Dunea

Mae French is fair, fat, and frequently hears voices. She has a flat affect and regularly fails to take her asthma drugs. Otherwise she does not strike you as being particularly disturbed, at least not on a cursory encounter. She finds the voices annoying and wishes they would go away.

Mae is under two psychiatrists whom she visits in a truly double blind randomised fashion. Their failure to communicate with each other must be blamed on the circumstance that neither one knows of the other's existence. Their joint efforts, however, have resulted in Mae taking at various times chlorpromazine, haloperidol, thioridazine, and fluphenazine—to little avail.

Meanwhile the illustrated magazines that keep us up to date report that "Clozaril" is a medical breakthrough for schizophrenia. The headlines in the financial newspaper announce that "Clozaril treats schizophrenia but kills people." The throwaways confirm the news. No need to look up the peer reviewed literature or send the latest student victim to do a computer search.

We learn later that clozapine is a dopamine receptor

antagonist that causes minimal elevation of prolactin levels and also has serotonergic, adrenergic, histaminergic, and cholinergic blocking activity. This is neither here nor there but could make nice slides for the two psychiatrists who haven't yet found each other. More to the point is a testimonial in a throwaway about a woman with schizophrenia who before treatment was dishevelled and had unsatisfactory hygiene (we never say dirty). She had all the symptoms in the book and they all improved dramatically with clozapine.

The drug is no panacea, it seems. Some 40% of patients are said not to respond, but it is more effective than the older drugs. In one study 32% of patients with refractory schizophrenia improved compared with 2% with chlorpromazine. Extrapyramidal reactions are rare, and most other side effects are acceptable. In 2% of patients, however, agranulocytosis develops, and 43 people have died in Europe.

Yet Mae's two psychiatrists would undoubtedly agree that her condition warrants a trial of the drug. Better than roam the streets of Chicago in the winter and be counted as one of the homeless by the liberal

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establishment. Unfortunately, the drug is exorbitantly expensive. In Europe it can be bought for as little as \$400 a year. In America the malpractice lawyers, legislators, and regulators have driven up the price to \$9000.

It seems that in order to avoid liability suits and to help have it approved the manufacturers proposed, and the regulators acquiesced, that the drug would be made available only as part of a total management package. This is administered by a subsidiary of a medical supplies company that sends a technician to draw blood for white cell counts each week and dispenses the drug according to the results. The system protects the manufacturers and the bureaucrats. It also provides the middleman with a profit not to be sneezed at. But the outcome is that the poor, and many not so poor, will have to go without the drug.

It is now deemed safe to sleep under a full moon.

Of course there has been talk of the state picking up the tab for the indigents, either voluntarily or as a result of a class action suit. Either way, this episode goes a long way to explain why by the year 2000 the cost of medical care is expected to rise to \$5000 a year for every American, a total of \$1.6 trillion, or 15% of the total national product. Much of this money goes to administration (20%), regulators, inspectors, paperwork, lawyers, malpractice premiums (\$4.5 billion) and above all to the enormous hidden cost of defensive medicine (\$12-14 billion).

Thus in a financial newspaper this year an internist working in a 430 bed hospital estimated the cost of complying with regulations and mandated paperwork in his hospital at \$8 million a year.¹ The hospital has an administrative supporting staff of 140 people who review charts, duplicate documents for outside agencies, or work in medical records or other offices to comply with all the requirements. In addition there are countless hours spent on paperwork by doctors, nurses, pharmacists, and other professionals. I should add that recently three teams of inspectors, each representing a different watchdog, came to a certain hospital on the same day. They spent considerable time

fighting over who should view the patient records first.

Many pessimists, moreover, believe that matters will have to get worse before they get any better. Few think that Mae will get clozapine in our time. They console us with the thought that if Mae were to be put into an institution she would soon rise to a top administrative job. In most instances, they say, a flat affect and hearing voices should not interfere with writing regulations or carrying out routine inspections of hospitals. Putting the inmates in charge, so to speak, has been a wildly successful experiment with the educational establishment. It is highly effective, safer than clozapine, and illiteracy is the only troublesome side effect.

Putting the lunatics in charge of the asylum, however, is no longer possible. This is because most of the asylums have been closed and their former clients now wander freely about the town carrying brown paper bags and sleeping under bridges. There are likewise no more lunatics, modern science having disproved any effect of the moon on human behaviour, this despite the authority of Aristotle, Galen, and Pliny the Younger.² The moon does not seem to cause illnesses, it does not make babies mad, it does not even drive people to commit crimes. Even the dreaded risk of lycanthropy, of people being transformed into wolves, seems to be minimal. And the Neapolitan women standing naked in the moonlight to increase the size of their breasts would have done better to have consulted a plastic surgeon.

Equally misguided were the farmers who would not plant their fields or shear their sheep by moonlight. It is now deemed safe to sleep under a full moon, to gaze in the face of the moon, to expose your baby to the moon. Only the migration of the salmon and the spawning of certain sardine-like fish has been definitely related to the increased light of a full moon. Most reports on the effects on man are negative, as is a recent meta-analysis of all studies ever carried out. Incidentally, this analysis indicates that it would require some 60 000 subjects to demonstrate a statistically significant effect, a project now under consideration by our top regulators.

1 Marchasin: Hospital tells the cost of regulation. Wall Street Journal 1990 June 26.

2 Frasca M. Moon madness: folklore and fact. *Pharos* Summer 1990:12-4.

ANY QUESTIONS

What are the causes of a raised plasma urea concentration with unchanged creatinine concentration?

The causes may be classified into those associated with an increased rate of urea synthesis and those characterised by reduced urea clearance along with a normal glomerular filtration rate. Urea production is related to the rate of protein catabolism. Slightly raised plasma urea concentrations (up to 10 mmol/l) may result from catabolic states (fever, trauma, burns, surgery), from haemorrhage into the gut or tissues, or even from dietary indiscretion. Fast response to chemotherapy is another possibility but must be distinguished from direct toxic effects on the kidneys. Some tetracyclines, by blocking the use of amino acids for protein synthesis, promote deamination and urea production.

A reduction in urea clearance due to functional renal insufficiency (as opposed to intrinsic renal disease) may occur when urine flow rates are reduced below 2 ml/min in hypovolaemic states. This reduction is due to the reabsorption of urea from the slower flowing tubular fluid, but for creatinine, which is not reabsorbed, the clearance remains normal. Plasma urea concentration will therefore

become raised in the presence of a normal creatinine concentration. Hypovolaemic conditions causing this pattern of results will comprise dehydration, shock, and blood loss, but other conditions provoking maximal conservation of sodium cations and water, such as increased renal vascular resistance or congestive heart disease, might be considered.

When the haemodynamic changes become sufficiently severe to produce a reduction in renal blood flow the glomerular filtration rate will fall and plasma creatinine concentration will also begin to rise. There will, however, be a disproportionately greater rise in the plasma urea concentration. An effective laboratory test for distinguishing prerenal azotaemia from acute renal failure is the fractional excretion of sodium. During the early stages of incomplete bilateral urinary obstruction a similar pattern of disproportionately greater rise in urea compared with creatinine concentrations is also seen. — K O LEWIS, *principal biochemist, Dudley Road Hospital, Birmingham*

Finn WF. Diagnosis and management of acute tubular necrosis. In: Mandal AK, Hebert LA. eds. *The medical clinics of North America. Renal disease*. New York: W B Saunders, 1990.