

and five years after the birth of the last child routine recall should start. The fall in detection rates among women repeatedly presenting themselves for rescreening is so dramatic¹² that a limit could be put on rescreening.

Multiphasic screening has already been criticised,¹³ and the Canadians agree that it is not realistic. For example, to link cervical screening with screening for breast cancer is unreasonable, because the epidemiological characteristics of women in the high risk group for cervical cancer are completely different from those of women at high risk for breast cancer, but the two might be linked when the women concerned reach 50 years of age. Nevertheless, this would link the finding of a condition which can be reasonably expected to be prevented or cured with a condition which is invasive at the time of detection and probably will not be cured. The detection of a few cases of unsuspected endometrial cancer is a bonus seldom mentioned in cervical screening.

That cervical cancer is a disease which can be limited successfully and even prevented is the conclusion of the Canadian report. Nevertheless, a high incidence of the disease is found¹⁴ in known and unknown defaulters to a screening programme, and also a significant number of cases occurs in women who have been inadequately screened. A few cases of cervical cancer will therefore always occur.

¹ *Canadian Medical Association Journal*, 1976, **114**, 1003.

² Cochrane, A L, Holland, W W, *British Medical Bulletin*, 1971, **27**, 3.

³ *Screening as a Tool of Preventive Medicine. Report by a Working Party 1972-74*, Strasbourg, Council of Europe—European Public Health Committee, 1974.

⁴ Department of Health and Social Security, *Seek Wisely to Prevent*, ed J Wakefield. London, HMSO, 1972.

⁵ Beral, V, *Lancet*, 1974, **1**, 1037.

⁶ Macgregor, J E, and Baird, D, *British Medical Journal*, 1963, **1**, 1631.

⁷ Boyes, D A, Fidler, H K, and Lock, D R, *British Medical Journal*, 1962, **1**, 203.

⁸ Aitken-Swan, J, and Baird, D, *British Journal of Cancer*, 1966, **20**, 642.

⁹ Yule, R, *Acta Cytologica*, 1972, **16**, 389.

¹⁰ Husain, O A N, et al, *Journal of Clinical Pathology*, 1974, **27**, 935.

¹¹ Macgregor, J E, *Cancer Cytology*, 1975, **15**, 1.

¹² Macgregor, J E, *Symposium of the Royal College of Pathologists*, 1975.

¹³ Knox, E G, *Lancet*, 1974, **2**, 1434.

¹⁴ Macgregor, J E, and Teper, S, *Lancet*, 1974, **1**, 1221.

Amenorrhoea after oral contraceptives

It is now ten years since the first accounts of amenorrhoea after the use of oral contraceptives were published.¹⁻⁴ Looked at in one way the condition seems trivial. Of itself it is not dangerous and does not impair health. Only two or three out of every hundred women who take oral contraceptives will develop post-pill amenorrhoea.⁵ But when it is considered that probably not less than a million women are taking oral contraceptives in Britain today, the figure becomes more impressive.

The incidence of post-pill amenorrhoea depends partly on its definition. In one recent study⁶ 89% of women began menstruating within 60 days of stopping the pill and all eventually had spontaneous periods. The incidence of 2-3% is a consensus taken from reports defining post-pill amenorrhoea as absence of menses for more than six months after stopping the pill. Naturally the amenorrhoea cannot be attributed to the pill in every case. A number of women have oligomenorrhoea before going on contraceptives, and it is likely that in many of these the post-pill amenorrhoea is merely the

continuation of a pre-existing condition. The incidence of pre-existing oligomenorrhoea varies in different studies of post-pill amenorrhoea, but it would be fair to say that about half the women who present with post-pill amenorrhoea showed some failure of menstruation before starting the treatment.

There is no way of proving that oral contraceptives will disrupt a fragile pituitary-gonadal axis. At best the injunction that women subject to bouts of oligomenorrhoea should not be put on oral contraceptives is based on a likely supposition. At worst it deprives them of efficient and convenient contraception for no very good reason. Late onset of the menarche is strongly correlated with post-pill amenorrhoea,⁶ and this, as much as oligomenorrhoea, should induce caution before starting a young woman on oral contraceptives.

The aetiology of post-pill amenorrhoea remains obscure. It is generally believed to be due to an effect of the oestrogen-progestin mixture on the hypothalamus, but this does not explain the cause of the condition. A recent suggestion that it is associated with a failure of the positive feedback to the hypothalamus by ovarian oestrogen⁷ carries the matter a little forward and implies a therapeutic possibility. The earliest studies showed that some patients with post-pill amenorrhoea also had galactorrhoea. Evidence of a failure of production of the hypothalamic prolactin-inhibiting factor comes up again and again. Prolactin assays are now widely available and hyperprolactinaemia is a more secure indication of a fault in the control of the secretion of this hormone than is galactorrhoea. Hyperprolactinaemia is often amenable to treatment with bromocriptine. It has become important to work out what part aberrations of prolactin secretion play in post-pill amenorrhoea. Although possibly we are dealing with two discrete conditions, it seems more likely that there is a continuous spectrum, only part of which is associated with hyperprolactinaemia. There is no case for blind treatment with bromocriptine without demonstrated prolactin excess.

In the absence of any other evidence of endocrine disease there is no strong reason for the investigation of post-pill amenorrhoea in the first six months after discontinuing oral contraceptives. Thereafter the investigative routine might well be influenced by whether or not the woman wishes to have a child. Nor is the presence of post-pill amenorrhoea a sufficient reason for omitting the usual infertility investigations—seminal analysis, tubal insufflation, and so on. Although some investigators have considered assays of pituitary gonadotrophins to be useful in the investigation of post-pill amenorrhoea, the case is not well proved except for detecting the occasional case of early menopause. If patients are near menopausal age or complain of hot flushes, high levels of follicle-stimulating hormone confirm the diagnosis of premature menopause. It is also unwise to subject any patient to treatment with pituitary gonadotrophins without first doing an FSH assay. Prolactin assay is mandatory if galactorrhoea is present and may be useful in any case.

It has been suggested that an oestrogen assay should be done, since patients with low levels of oestrogen should be treated with gonadotrophins and those with moderate or high levels treated with clomiphene. This may be an oversimplification. Oestrogen assays may give a useful indication of the degree of ovarian activity, but they are at best only a rough guide to the choice of treatment and are not a secure means of sorting patients into categories. As induction of ovulation with anti-oestrogens is so much simpler and less dangerous than treatment with gonadotrophins, it is advisable to try this first in most cases.

At present bromocriptine treatment should be reserved for patients with raised plasma prolactin concentrations. Even patients who, on x-ray examination of the pituitary fossa, have been shown to have small adenomata, often respond to bromocriptine. Such women should be carefully watched. They readily become pregnant and occasionally sudden enlargement of the tumours leads to visual defect. Induction of ovulation with antioestrogens such as tamoxifen or clomiphene is still the first line of treatment for patients with sterility associated with post-pill amenorrhoea; pituitary gonadotrophins are a last resort.

Post-pill amenorrhoea does not threaten health and is seldom permanent unless it is incidental to other causes of secondary amenorrhoea. Judged by the yardstick of successful pregnancy the outlook is less rosy. Although upwards of 80% will ovulate with treatment, in a recent study only 22 live births were obtained among 50 treated patients.⁹

¹ Shearman, R P, *Lancet*, 1966, **2**, 1110.

² Whitelaw, M J, Nola, V F, and Kalman, C F, *Journal of the American Medical Association*, 1966, **195**, 780.

³ Gregg, W I, *New England Journal of Medicine*, 1966, **274**, 1432.

⁴ *British Medical Journal*, 1972, **4**, 59.

⁵ Golditch, I M, *Obstetrics and Gynecology*, 1972, **39**, 903.

⁶ Evrard, J R, Buxton, B H, and Erikson, D, *American Journal of Obstetrics and Gynecology*, 1976, **124**, 88.

⁷ Marshall, J C, Reed, P I, and Gordon, H, *Clinical Endocrinology*, 1976, **5**, 131.

⁸ Furuholm, M, and Carlström, K, *Acta Obstetrica et Gynecologica Scandinavica*, 1973, **52**, 373.

⁹ Grant, A, *International Journal of Fertility*, 1973, **18**, 44.

How long dead?

One of the fascinations of forensic medicine is that it makes excursions into other disciplines such as anthropology, dentistry, radiology, botany, and even zoology. An instance vital to the investigation of a crime was given by Mr Justice Cusack in a recent address to the Medico-Legal Society.¹ He described how entomology had contributed to the conviction for murder of William Brittle, now serving a life sentence for a killing in Gloucestershire in 1965. His victim was murdered by a "commando punch" to the throat in a lonely bungalow and was transported in the boot of Brittle's car to Bracknell, in Berkshire. The body was imperfectly buried under leaves and debris, and small boys searching for fishing maggots came across a prolific supply, which led to the discovery of the body. This was 12 days after the victim had last definitely been seen alive, but the prosecution case was hampered by other witnesses who claimed to have seen him alive in the interim. The case against Brittle was so unsatisfactory that the Director of Public Prosecutions declined to bring him to trial, and eventually it was a coroner's jury that committed him to the assizes.

Much of the case rested on the time that had elapsed since death, and this was established within fairly close limits by the stage of maturity of the bluebottle maggots on the body. The offspring of bluebottles pass through the egg stage, three successive larval stages called instars, and finally become pupae before they emerge as winged insects. Though there is appreciable variation due to climatic conditions—as well as some minor differences of opinion among entomologists—the whole cycle usually takes 22 days, and large final instar maggots may be expected at around the 10-12th day. In

Brittle's case the entomological evidence fitted well within the time of death alleged by the prosecution and excluded some of the alleged sightings of the victim by other witnesses.

The case highlights the great difficulties of assessing the time of death. Even in the first 24 hours estimations from temperature and other factors are fraught with gross inaccuracies. Probably more has been written about time-since-death than any other single subject in forensic pathology, but many so-called improvements in technique have not withstood critical evaluation. When a considerable delay occurs before the discovery of a dead body the problem becomes even more difficult, since environmental conditions are of paramount importance in modifying the process of decomposition—temperature, moisture, animal predators—and the physical surroundings of the body so distort the chronology of putrefaction that accuracy becomes unattainable.

Bluebottle infestation was used as a time-marker in another famous murder, when Dr Buck Ruxton, a Lancaster general practitioner, murdered and dismembered his wife and housemaid in 1935. Again, the age of the largest larvae could not have exceeded 12 days, and the time of death was narrowed down considerably. As well as variations in the length of the cycle with climatic and other conditions, however, another important factor is the time at which the first eggs are laid. The adult fly tends to prefer fresh tissue as opposed to already badly decomposed material, but there may be a delay of a day or more, again depending upon environmental factors. Conversely, eggs may sometimes be laid on the living body, especially if the victim is unconscious or debilitated, when flies may infest eyelids, nostrils, and wounds: so that here as in many other facets of legal medicine dogmatic statements should be avoided.

Animal infestation may make a profound difference to the rate of decomposition. As well as being a marker of the time of death the presence of fly larvae greatly increases the rate of decomposition, owing to the secretion of proteolytic enzyme which penetrates the skin and liquefies the tissue. Other insect predators and even larger animals such as rats, foxes, and dogs may contribute to the irregular progress of decomposition. Since these factors can never be completely within the knowledge of the pathologist further inaccuracies are inevitable.

When putrefaction and predators have done most of their work, the problem of determining the time since death becomes more difficult when the discovered remains are mostly skeletal. If any soft tissue such as cartilage, tendon, or periosteum is found, then death probably took place within the last year or two, though again seasonal and climatic changes must be taken into account. When the examiner is confronted with dry bones the problem becomes even more difficult. Paradoxically, the archaeologist may be able to achieve a better accuracy percentage with bones which are thousands of years old than the forensic pathologist with bones only a few score years after death. With ancient bones the remarkable (if expensive) radiocarbon analysis can give a relatively accurate dating. On the other hand, in bones recent enough to be potentially of forensic importance the radiocarbon test is of no help, and considerable effort has been made recently to develop chemical, physical, and serological tests to increase the accuracy of their dating. Nevertheless, the dominance of environmental factors in altering the decay pattern of skeletal material makes it unlikely that we shall ever attain any great accuracy.

¹ *Medico-Legal Journal*, 1976, **44** (2), 48.