Effective concentration of the spermatozoa can be achieved by using the first portion of the split ejaculate, and again the cervical insemination cap may be used to keep the semen specimen in contact with the cervix overnight. Alternatively, the semen may be introduced directly into the lower cervical canal.

Although a small volume of semen can be introduced direct into the uterine cavity, it may prove highly irritant; spermatozoa should be separated from the seminal plasma before intrauterine insemination. Centrifugation with an equal volume of normal saline, and resuspension of the precipitate, will remove the irritant plasma but retain the dead spermatozoa and other debris as contaminants. The motile spermatozoa will swim free if the suspension is layered on top of a 10% low-salt human serum albumin column for an hour.

When the sperm count is low banking consecutive specimens of semen in liquid nitrogen will further concentrate spermatozoa and so build up a "deposit account" that can be used at the appropriate time of the wife's menstrual cycle. Such banking may be carried out with neat semen, the first portion of the split ejaculate, or isolated spermatozoa.

Verdicts on the success of these techniques range from total disappointment to extreme optimism, but studies are not usually comparable because of the lack of objective definitions of semen quality or the techniques used. We need uniform criteria if we are to assess the value of the more complex AIH procedures.

Another problem is the pregnancy wastage that may occur; Moghissi *et al*[1] recently reported that some half of pregnancies resulting from AIH ended in an abortion during the first trimester. Most clinicians, indeed, believe that there may sometimes be a relation between subfertile semen and miscarriage, whether pregnancy occurs naturally or through AIH. Fortunately we have no evidence that the incidence of abnormality in completed pregnancies is raised. Moreover, at present AIH techniques seem a better approach to subfertility than the empirical use of drugs.

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Human beta-endorphin: the real opium of the people?

The idea that the brain produces an "endogenous analgesic" is based in part on the variation in our perception of pain in different circumstances. Indeed, pain perception may be completely suppressed for a while, as may occur with war wounds. Possibly, too, stimulation of the release of such a substance within the central nervous system by acupunture might be the basis for the relief of pain this treatment can provide.

The human brain contains receptors which will bind opium specifically. Normally these receptors probably modulate pain perception by reacting with a natural brain substance; only coincidentally do they bind the active principle of the opium poppy, which therefore acquires analgesic properties. Chronic opiate abuse would be expected to cause sustained suppression of the endogenous analgesic; so that suddenly depriving an addict of opiates would lead to receptors being unoccupied and the features of opiate withdrawal. Indeed, if acupuncture does stimulate the release of the "natural opiate" then it would explain the reported success of electroacupuncture in treating the symptoms of heroin withdrawal.[1 2] All these ideas, however, have remained speculative.

Hughes and his colleagues in Aberdeen reported in 1975 the identification of two small peptides extracted from porcine brain tissue which have strong opiate-like analgesic and receptor-binding activity.[3] These substances, the enkephalins, each contain five amino-acids and differ from each other only by one amino-acid. Soon after their discovery the structure of one of the enkephalins was noted to be identical to part of a much larger pituitary peptide hormone called beta-lipotrophin (β-LPH)[4 5]; and subsequently other peptides related to β-LPH, the endorphins, have been shown to have even greater affinities for the opiate receptors.[5–7] One of these, beta-endorphin, is at least 30 times more potent than enkephalin in its binding to opiate receptors and is a more powerful analgesic.

Beta-lipotrophin is found in the anterior pituitary in the same cells as corticotrophin (ACTH) and is secreted in parallel with it under both physiological and pathological conditions, yet its biological role has remained unknown.[8] Recent studies suggest, however, that β-LPH may be the precursor of the endorphins, the family of endogenous analgesics. We might expect that beta-endorphin would be secreted during stress along with ACTH.[9] Nevertheless, claims to have shown that beta-endorphin is secreted as a separate substance must be viewed with caution, since sufficient care has not always been taken to distinguish between intact β-LPH and the smaller free beta-endorphin peptide. The beta-endorphin sequence of amino-acids is contained within the β-LPH molecule, so that any antibody used in radioimmunoassay may detect the beta-endorphin sequence, whether present separately or as part of the larger molecule. Thus in the rat it has not yet proved possible to distinguish circulating beta-endorphin from β-LPH by routine radioimmunoassays unless a chromatographic step is introduced.[10] Reports of successful identification of beta-endorphin or enkephalin in the pituitary glands and other tissues of man or lower animals by histochemical and immunological techniques[11 12] should be treated with similar scepticism. The technical problems of dealing with solid tissues are even worse than with tissue fluids; in addition to the complicating factors already discussed β-LPH may break down during storage or extraction of tissues, generating beta-endorphin as an artefact.

In an attempt to overcome these problems in man Jeffcoate and his colleagues[13] have used two assays simultaneously, one for the part of β-LPH that contains the beta-endorphin sequence and another for the part that does not. The results of their studies in man have suggested that beta-endorphin may always be found in cerebrospinal fluid separate from the larger β-LPH. The identity of this beta-endorphin in the cerebrospinal fluid has been confirmed chromatographically.[13]

After removal of the pituitary in animals opiate agonist activity can still be found in brain tissue; this material resembles beta-endorphin.[14] Krieger and her colleagues[15] have reported the presence of β-LPH and ACTH in the brains of several species independent of the presence of the pituitary and suggested that their distribution may be dissociated. Jeffcoate *et al*[13] now have found beta-endorphin in the cerebrospinal fluid of patients with no LPH or ACTH in their blood owing to pituitary or hypothalamic disease. Hence these peptides may be synthesised directly in the brain instead of exclusively in the pituitary, as has been assumed. Furthermore, the premise that synthesis of ACTH and β-LPH always occurs together (as appears to hold for the pituitary gland) may not be true for the brain.

The physiological roles of brain ACTH, β-LPH, and beta-endorphin are likely to be different from their counterparts derived from the pituitary: they may, indeed, have to be considered more as neurotransmitters and behaviour modulators than as hormones. Peptide fragments of ACTH are known to alter behaviour in some mammalian species.[16] Like morphine, enkephalin and beta-endorphin act on hypothalamic mechanisms to cause the release of both growth hormone and prolactin in rats,[17] and an analogue of enkephalin has now been shown to have the same hormonal effects in man and in addition to lower gonadotrophin and ACTH concentrations.[18 19]

Immediate priorities in endorphin and enkephalin research may lie, then, not so much in attempts to study their alterations in the blood but instead in careful chemical and pharmacological characterisation of these substances in brain and CSF. Studies

on these lines may indicate the true physiological role of these peptides and their relation to pain perception and behaviour.

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Medical audit and continuing education

British doctors have accepted the need for postgraduate education but they still seem reluctant to introduce any more formal type of medical audit. The idea of measuring and evaluating the individual and collective quality of care provided by doctors is still viewed with scepticism and suspicion. Yet some controlled form of continuing education of physicians should be seen as essential—though done on a voluntary basis, whether by self-assessment or as peer review.[1] As part of this process the collection of data needs to be centrally organised, analysed, and interpreted. These problems were the subject of a recent symposium held at the Royal College of Physicians of Edinburgh.

The threat of sanctions implied by the term audit and the spectre of recertification for competence to practise have provoked anxieties both here and in the United States, where audit has been national policy for some years.[2 3] Recent assessments[4] of the work of the Professional Standards Review Organisation (PSRO) have found disappointingly little evidence of improvements in outcome. Last month the *New England Journal of Medicine*[5] suggested that Americans had been premature in their enthusiasm for PSRO reviews—"our profession has been asked to 'do something' before we have learned how."

Aspects of medical work such as the optimum use of ancillary investigations and the assessment of treatment can be readily evaluated, and audit of this kind has been a feature of medical practice for many years. Some of the newer proposals, however, go far beyond this and suggest measuring a doctor's skill in, for example, eliciting physical signs, accuracy of diagnosis, and doctor-patient relationships. The variability and disagreement among practitioners on these intangible matters are such, however, that acceptable methods of measurement will prove difficult to devise. The one certainty is that the medical profession will insist that it alone can properly evaluate the art as distinct from the science of medicine.

Medical audit has three main components: setting professional standards; assessing clinical performance; and modifying clinical practice.[1] Experience in the United States[3] indicates that audit may be a valuable educational tool but counter-productive when used punitively. Any process of audit, therefore, should be linked closely to continuing education. By no means all doctors take advantage of symposia, lectures, and clinical meetings; and those who do are often assumed to be the keen and enthusiastic faction—the rather cynical inference being that those who do not attend are in some way inferior. In truth there may be many reasons for non-attendance: difficulties in travel, inconvenience of time, or excessive service commitments. Furthermore, some individuals find the traditional type of teaching unattractive. For these reasons, the meeting heard that new techniques aimed at the widest possible participation are being developed at the Centre for Medical Education, University of Dundee. These use common methods of communication such as post, telephone, and domestic television. The emphasis is on self-assessment by doctors; this requires teaching material of a high standard with rapid and detailed feedback to the individual doctor. A major difficulty in assessing such programmes is that of itself participation can be no guarantee of successful continuing education. Some form of evaluation is needed; but confidentiality would need to be maintained to retain participants' confidence and to prevent dropout.

Peer assessment is a popular concept at present, but the details have yet to be worked out. Even if selection were controlled by professional organisations how many would recognise the "peers"? Another possibility is some form of compulsion on doctors to participate in formal teaching courses; again the likely response would be hostile and probably counter-productive.

Despite these practical problems medical audit should be seen as a responsibility rather than a threat. If adequate controls are maintained doctors can regard these new ideas as an exciting challenge that should improve standards of care. As a first step more needs to be done to organise the central collection of data. This requires commitment by clinicians and effective co-ordination by the colleges and specialty organisations. Central authorities should provide resources to encourage the profession to solve these problems—without legislation, regulation, or threat of recertification. If our American colleagues have pioneered the route we should make sure we benefit from their experience.

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