hypertension and microscopic proteinuria,[10] are not, of course, influenced by the type of surgery.

The traditional attitude to living donors in the United Kingdom has been understandably cautious. However, the severe shortage of cadaveric kidneys and the success of living donor programmes in other countries has led many British transplant surgeons and nephrologists to reconsider their views. We now need quantitative data on the potential for living donation to increase the transplantation rate in the United Kingdom and to determine the resource implications of such an expansion. Any increase in living donor transplantation must accord with the highest possible standards of clinical care. Establishing long term prospective follow up of all British donors would help to answer the criticisms of those who believe that unilateral nephrectomy is harmful even in healthy individuals.

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Delivering inhaled corticosteroids to patients

If side effects are important, why are we so ignorant of the dose inhaled?

Inhaled steroids play an extremely important part in the treatment of asthma. They are now regarded as the first line prophylactic drug for adults[1] and are used by many as a first line prophylactic agent for children. Important side effects are rarely seen in users of low dose inhaled steroids, but there is concern over the potential effects of high dose inhaled steroids. The Committee on Safety of Medicines has recently concluded that clinically important systemic adverse effects can occur at licensed doses of inhaled corticosteroids,[2] the risks being increased after prolonged high dose therapy. Effects mentioned included adrenal suppression, osteoporosis or changes in bone mineral density, growth retardation in children, cataracts, and glaucoma. A major problem in trying to identify possible side effects—and, indeed, in assessing clinical trials of inhaled steroids—is determining the amount of drug patients have actually inhaled. Compliance and inhaler technique vary considerably, but even when these are optimal the dose of drug inhaled may vary by up to fourfold without the patient, prescriber, researcher, or regulator being aware.

Studies on the effect of inhaled steroids usually quote the prescribed dose. This is simply the strength of inhaler times the number of doses a patient is taking. For example, two actuations of a 100 μg strength (the nominal dose per actuation) metered dose inhaler twice daily is 400 μg/day. Marketing inhalers of different strengths and not making clear which is which on the label is forbidden by the Medicines Control Agency. However, when nebuliser and spacer devices are used the prescribed dose may bear little resemblance to the dose actually available for the patient to inhale—the received dose.

In the United Kingdom drug delivery devices made outside pharmaceutical companies may be marketed without a licence and sold to the general public. The manufacturers of such devices do not have to provide information on the amount of drug the patient is likely to receive when using their device, and pharmaceutical companies are required to provide information on drug delivery devices only if they recommend a specific device for their product.

The type of device used may affect the delivery of inhaled steroids. For instance, beclomethasone dipropionate administered by nebulisation actually delivered a fraction of a similar nominal dose delivered by large volume spacer.[3] Major differences in the dose inhaled may also occur between devices of the same class. We have recently found that the dose of budesonide a 10 year old patient may inhale from a "breath enhanced, open vent" nebuliser is four times that available from an "open vent" device and twice that available from a conventional nebuliser (unpublished). Parents buying a nebuliser will be totally unaware that the dose of steroid their child will inhale may vary by a factor of four depending on their choice of nebuliser.

The effect of the drug delivery device used on the level of side effects is rarely taken into account when evaluating side effects. In many published studies it is not clear how patients took their medication. For example, a recent study identified a possible association between the use of inhaled steroids and the development of posterior subcapsular and nuclear cataracts.[4] Higher cumulative lifetime doses of beclomethasone dipropionate were associated with higher risks of posterior subcapsular cataracts, the highest prevalence (27%) being found in subjects whose

BMJ 1999;318:410–1

lifetime dose was over 2000 mg. It would be of interest, and reassuring, to know whether patients using a spacer device had a lower incidence of side effects. Spacer devices used with pressurised metered dose inhalers reduce oropharyngeal deposition of aerosolised steroids,[5] and hence the total body dose, without affecting the dose delivered to the airways. Their use has been documented to reduce hypothalamic-pituitary axis suppression by beclomethasone dipropionate,[6] and the British asthma guidelines recommend their use for the delivery of inhaled steroids.

Without information on the likely dose of drug inhaled, the results of clinical trials may also be misinterpreted.[7] If more than one type of nebuliser or spacer is used in a trial the results should not be pooled as patients will probably have received different doses. The practice of subjecting patients to the risks and inconvenience of a clinical trial without taking the confounding effect of different drug delivery devices into account should be questioned. Similarly, regulatory authorities should review the information required of the manufacturers of drugs and drug delivery devices about the delivery of inhaled steroids. This may help in interpreting trial data for therapeutic effect and possible side effects. Advisory bodies on asthma management may also be able to give more informed information to both prescribers and patients.

Although significant side effects are apparently rare in users of low dose inhaled steroids, information on the dose of drug inhaled is of therapeutic importance. Patients are being prescribed inhaled steroids at younger ages, and lifetime doses may greatly exceed those reported in the current literature. Current advice remains that the dose of inhaled steroid, whatever the delivery device, should be titrated to the lowest dose at which effective control of asthma is maintained.

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Radiosurgery for brain tumours

Triumph of marketing over evidence based medicine

Recent publicity surrounding the opening of a private radiosurgery facility in the United Kingdom suggested near miraculous properties for a radiation technique developed over 30 years ago. According to media reports, "many potentially fatal brain conditions which are inoperable using conventional surgery can now be treated successfully."[1] This form of marketing is misleading and offers false hope.

Radiosurgery is a term applied to high precision localised irradiation given in one session. One technique uses cobalt sources arranged in a hemisphere and focused on to a central target (described as a gamma knife). A gamma knife unit has been in operation in Sheffield since 1986. Identical high precision radiosurgery can be delivered by appropriately adjusted linear accelerators and has been available in Britain since 1989. Currently, at least six radiosurgery facilities are available to NHS patients. The limited usefulness of the technique for treating brain tumours suggests that the existing NHS facilities are sufficient for the expected workload.

The aim of radiosurgery is to deliver a sphere of high dose irradiation more localised than would be achieved with conventional radiotherapy. However, this is possible only for small lesions less than 3.5-4 cm in diameter. Radiosurgery was used initially for treating inoperable arteriovenous malformations and subsequently for treating acoustic neuromas, solitary brain metastases, and a mixture of other tumours. Despite many years of experience, there is no single randomised trial or robust case-control study testing the efficacy and safety of radiosurgery in comparison with other established treatments. Most reports claiming benefit are from retrospective studies of enthusiastic application of radiosurgery to patients with small brain tumours.

It is generally agreed that single fraction radiosurgery obliterates 80-90% of small arteriovenous malformations. The aim is to reduce the risk of subsequent haemorrhage from an annual untreated rate of rebleeding of 2-4%. In the first two years after radiosurgery the reported annual rebleeding rate is 4-8%,[2 3] and long term data on the incidence of rebleeding at 5-10 years are poor. No information exists on the survival of treated compared with untreated patients. The treatment is not without toxicity: the risk of radiation induced damage seen on magnetic resonance imaging is 20-30% for 2 cm and 40-50% for 3 cm diameter lesions, and these are often symptomatic when in eloquent regions of the brain.[4]

The tumour control of acoustic neuroma after radiosurgery is 91% at five years with a 17% risk of VIIth and a 45% risk of VIIIth neuropathy at five years.[5] Radiosurgery has been advocated for patients with other benign tumours. Early results suggest a recurrence rate of small benign meningiomas of $>10\%$ at five years with a 6% risk of neurological toxicity.[6] Long term tumour control of pituitary adenoma after radiosurgery is not known. However,

BMJ 1999;318:411–2