Letters

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Intranasal corticosteroids in allergic rhinitis

Paper did not include all data on adverse effects

EDITOR—Weiner et al conclude that "results from [their] systematic review, together with data on safety and cost effectiveness, support the use of intranasal corticosteroids over oral antihistamines as first line treatment for allergic rhinitis."[1] They also state that "intranasal corticosteroids are considered safe [and] studies have failed to show significant effects on serum markers of bone metabolism and short term bone growth," referring to two studies, those by Martinati et al and Wolthers et al. They make no reference to two more recent studies, both of a larger number of subjects over longer periods, which established a significant reduction in paediatric bone growth.[2 3]

The issue of adverse effects was also addressed in a report by the Committee on Safety of Medicines and Medicines Control Agency, which concluded that intranasal corticosteroids can cause "clinically important systemic adverse effects at licensed doses." [4] The United Kingdom datasheet for Beconase aqueous nasal spray (beclomethasone dipropionate) recognises the potential for children to develop growth retardation at licensed doses and the need to refer patients to paediatric specialists while they are being prescribed intranasal corticosteroids (Allen and Hanburys, Sept 1998).

I question the omission of such key data from Weiner et al's systematic review; it may well tip the risk:benefit ratio away from the use of intranasal corticosteroids in children and, hence, affect the validity of the review's conclusions.

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1 Weiner JM, Abramson MJ, Puy RM. Intranasal corticosteroids versus oral H_1 receptor antagonists in allergic rhinitis: systematic review of randomised controlled trials. *BMJ* 1998;317:1624-9. (12 December.)
2 Wolthers OD, Pedersen S. Short term growth in children with allergic rhinitis treated with oral antihistamines, depot and intranasal glucocorticoids. *Acta Paediatr* 1993;82:635-40.
3 Rachelefsky GS, Chervinsky P, Meltzer EO, Morris RM, Seltzer JM, Skoner DP, et al. An evaluation of the effects of beclomethasone dipropionate aqueous nasal spray [Vancenase AQ (VNS)] on long term growth in children. *J Allergy Clin Immunol* 1998;101:S236. (Abstract 979.)
4 Committee on Safety of Medicines/Medicines Control Agency. The safety of inhaled and nasal corticosteroids. *Curr Probl Pharmacovig* 1998;24:8.

Evidence of efficacy is useful but not only factor to be considered

EDITOR—The headline "Intranasal corticosteroids should be used for allergic rhinitis" in This week in the BMJ gives a useful evidence based message for busy practitioners. Unfortunately, this message cannot properly be concluded from the paper concerned, which is a systematic review of randomised controlled trials comparing the efficacy and cost effectiveness of intranasal steroids and oral antihistamines.[1] The evidence from this review is useful, but evidence on several other issues needs to be weighed up before we can conclude that intranasal steroids should be used.

Patient centred consultations, in which therapeutic decisions are the result of negotiation between the health professional's expert medical knowledge and the patient's expert knowledge about himself, also require evidence about other treatments and about adverse effects. Other treatments for allergic rhinitis include allergen avoidance measures, allergen immunotherapy, and homoeopathy. Although these non-pharmaceutical alternatives may have slower and less powerful effects, they may be chosen by patients who wish to avoid the risks inherent in drug treatment or used alongside drug treatment, thereby reducing the dose required.

The issue of adverse effects is of central concern to many patients but is often treated dismissively by health professionals. Weiner et al's paper introduces the topic with the statement "Intranasal steroids are considered safe." Considered safe by whom? Certainly not by patients, who often have deep seated anxieties about corticosteroids. Nor are they considered safe by the Committee on Safety of Medicines and the Medicines Control Agency, which concluded that clinically important systemic adverse effects can occur.[2] They identified five main areas of concern: adrenal suppression, osteoporosis or changes in bone mineral density, growth retardation in children, cataracts, and glaucoma. Although this was published as an unreferenced report, the authors supplied me with the list of 123 references on which it was based. Some case reports that illustrate these problems have also been published recently.[3]

To suggest that evidence from a systematic review of the efficacy of two treatment options is sufficient for evidence based therapeutic decision making is an oversimplification and is not in keeping with the concordance model of prescribing.[4] Patients and their doctors need a wide range of evidence for their problem solving,[5] and even then factual knowledge will be only one of many inputs that guide their decisions.

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1 Weiner JM, Abramson MJ, Puy RM. Intranasal corticosteroids versus oral H_1 receptor antagonists in allergic rhinitis: systematic review of randomised controlled trials. *BMJ* 1998;317:1624-9. (12 December.)
2 Committee on Safety of Medicines/Medicines Control Agency. The safety of inhaled and nasal corticosteroids. *Curr Probl Pharmacovig* 1998;24:8.
3 Findlay CA, Macdonald JF, Wallace AM, Geddes N, Donaldson MDC. Childhood Cushing's syndrome induced by betamethasone nose drops, and repeat prescriptions. *BMJ* 1998;317:739-40. (12 September.)
4 Royal Pharmaceutical Society of Great Britain. From compliance to concordance: towards shared goals in medicine taking. London: RPS, 1997.
5 Paterson C. Problem setting and problem solving: the role of evidence-based medicine. *J R Soc Med* 1997;90:304-6.

Authors' reply

EDITOR—Our review concluded that intranasal corticosteroids are more effective than oral antihistamines in the treatment of allergic rhinitis. We also presented data showing that intranasal corticosteroids are more cost

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effective. The authors of these two letters refer only to the third issue raised in our paper, that of safety.

The Committee on Safety of Medicine's publication *Current Problems in Pharmacovigilance* is a drug safety newsletter sent to doctors, dentists, pharmacists, and coroners in the United Kingdom. The unreferenced summary about the safety of inhaled and nasal corticosteroids that both Paddon and Paterson refer to makes no distinction between inhaled and intranasal corticosteroids—a fact cited incorrectly by Paddon and not mentioned by Paterson. In fact the article goes on to state that "the risks with intranasal corticosteroids are generally lower than with inhaled steroids." We note that there are warnings about the safety of terfenadine and astemizole in the December 1997 and February 1999 editions respectively.

Paterson cites the cases reported by Findlay et al.[1] These authors reported on two patients who developed Cushing's syndrome while taking betamethasone nose drops; they also found four similar case reports for the 18 years from 1980, concerning three patients taking betamethasone and one taking dexamethasone nose drops. These agents have a high potential for systemic bioavailability, and our systematic review did not include any comparison with these agents.

Paddon cites two studies on short term bone growth. One is reported in an abstract,[2] and we have been unable to find a reference to a complete paper. The other is a 1993 paper by Wolthers and Pedersen,[3] and we cited their 1994 paper.[4] Paddon is incorrect when he states that the 1993 paper reported on more subjects taking intranasal corticosteroids (11 subjects) than the 1994 paper did (27 subjects). All clinicians prescribing intranasal corticosteroids should be aware that the unresolved issue regarding growth is under scrutiny.

Intranasal corticosteroids have had an outstanding safety record in 25 years of use. To our knowledge, no deaths have been recorded, which is more than can be said for oral antihistamines. Indeed, a recent report of a prolonged QT interval and arrhythmia with fexofenadine may well tip the risk:benefit ratio further away from the use of oral antihistamines.[5]

Once an intervention is recommended from evidence based data it is incumbent on the clinician to decide on the dose, duration of treatment, follow up, and risk:benefit ratio in consultation with the patient.

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Are African governments allocating sufficient resources to fight AIDS?

Editor—The editorial by Wilkinson et al addresses the important question of programmes to prevent perinatal transmission of HIV in Africa.[1] The authors highlight the prohibitive cost of zidovudine and suggest that placebo controlled trials should be revived.

Since the prevalence of HIV infection among pregnant women is above 30% in some parts of South Africa (A Smith, HIV-AIDS update symposium, Durban, Natal, South Africa, January 1999), AIDS is now the biggest threat to African society. Thus we must ask whether African governments are allocating sufficient resources to meet the challenge.

Data from the UNAIDS perinatal transmission trial, which were released in Chicago in February, showed that shorter and cheaper regimens using zidovudine and lamivudine work just as well as the AIDS clinical trials group's protocol 076. Given that GlaxoWellcome has reduced the cost of these drugs by 75%, one wonders just how little these drugs will need to cost before any African government implements a national programme to prevent perinatal transmission of HIV.

The real problem in Africa is the failure to deliver adequate health care. Even if zidovudine and lamivudine were made available, the limitations of the infrastructure would still be a stumbling block to reducing perinatal transmission of HIV. We know from the directly observed treatment short course (DOTS) programmes for tuberculosis that "free drugs" have failed to eradicate this disease for similar reasons.[2]

The fact that zidovudine "costs far more than most African countries spend per head on health" is true but the situation can change. In this decade more wars have been financed in Africa than in the previous decade, and there is the added financial burden of debt servicing. Perhaps it is time to write off old debts and earmark any future aid for the sole purpose of reducing the perinatal transmission of HIV, treating tuberculosis, and financing public health programmes.

High mortality among mothers and children was the norm in Africa even before AIDS because of the poor infrastructure and the meagre resources allocated to health care. The call for more placebo controlled trials must not be heeded. The evidence for the effectiveness of non-drug interventions in preventing mother to child transmission of HIV is weak.[3]

AIDS in Africa needs an African solution: an appropriate political and economic response.[4]

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Impact of HIV infection and AIDS on prevalence of type 2 diabetes in South Africa in 2010

Editor—Many non-communicable diseases are set to increase dramatically during the 21st century. In particular, the prevalence of diabetes mellitus may double from 124 million people worldwide in 1997 to 220 million by 2010.[1] Regions with the greatest potential increases are Asia and Africa—precisely the areas with the greatest potential increases in the prevalence of HIV infection and AIDS. The impact of HIV infection and AIDS on the diabetes epidemic is difficult to assess, but we have tried to estimate it for South Africa using population data from the United Nations[2] and estimates of the prevalence of diabetes (table).[1 3]

The population will continue to increase but at a slower rate because of the HIV/AIDS epidemic. South Africa's annual growth rate, which was 1.9% in 1995, is expected to decrease to 0.3% in 2010. Without HIV/AIDS it would be 1.5%. The highest age specific prevalence of HIV infection is forecast for those aged 20-34 years.[4] Amos et al predict that the age adjusted prevalence of type 2 diabetes will increase from 1.7% to 3.7%, resulting in 1 624 000 cases in 2010.[1] A less conservative prevalence of 4% rising to 8% gives an estimated 3 482 000 cases, occurring mainly in those aged 50-59 years. When the effect of HIV/AIDS on population growth is calculated this number is predicted to decrease to about 3 380 000 cases, a 3% reduction representing over 100 000 fewer cases of type 2 diabetes.

Although the interaction of two diseases that might affect various subgroups of the South African population differently is difficult to model, the burden of both HIV/AIDS and type 2 diabetes is likely to fall on the lower socioeconomic classes. The peak age specific prevalence occurs earlier in HIV/AIDS than type 2 diabetes, but correspondingly fewer infected people will survive to middle age. Thus our calculation of 3% fewer cases, reflecting the expected

Demographic impact of HIV infection and AIDS on projected prevalence of type 2 diabetes in South Africa

		2010	
Reference	**1995**	**Without HIV/AIDS**	**With HIV/AIDS**
United Nations[2]			
Population (×1000)	41 464	43 529	42 256
Growth rate (%)	1.9	1.5	0.3
Amos et al[1]			
Type 2 diabetes:			
Prevalence (%)	1.7	3.7	3.7
No of cases (×1000)	717.8	1624.0	1576.1
Levitt and Mollentze[3]			
Type 2 diabetes:			
Prevalence (%)	4.0	8.0	8.0
No of cases (×1000)	1658.5	3482.3	3380.5

decrease in population growth due to HIV/AIDS, represents a small but substantial reduction, irrespective of the prevalence of diabetes selected. This figure may actually be higher if the indirect effects of AIDS are considered, such as the decrease in obesity because of chronic infection and wasting. This will ameliorate insulin resistance and better preserve residual β cell function.[5] The toll of HIV/AIDS on mortality, population loss, and diabetes prevalence may even be greater elsewhere in Africa.

Our model highlights the need to adjust for the impact of HIV/AIDS when projecting the prevalence of chronic diseases and national health budgets into the next century.

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Use of randomisation in early clinical trials

Theobald's trial in 1936 incorporated some aspects of randomisation

Editor—The issue of 31 October marking 50 years of the randomised controlled trial, with historical accounts on trial methodology, made me look up the trial undertaken by Theobald. He studied the combined effect of calcium, vitamin A, and vitamin C supplementation on toxaemia in 100 pregnant women, apparently using true individual randomisation.[1 2] This was in 1936, a decade before the streptomycin trial.[3]

Although not all aspects of the randomisation procedure are entirely clear from Theobald's report,[1 2] he was obviously a thoughtful researcher. He provided evidence that the groups had similar age and parity distributions, had a statistician (E S Pearson) to assess the extent to which his results (that symptoms of toxaemia were less common in the treatment group) could have arisen by chance, and even used blinding of the primary outcome assessors. Despite these facts Theobald's trial seems to be little cited in the literature.

Another London trial is interesting from a methodological point of view. During 1938-9 the People's League of Health allocated over 5000 pregnant women from 10 hospitals to receive either no supplement or a supplement containing calcium, vitamin A, and vitamin C as well as other substances.[4 5] The trial was an enormous achievement, not only because of its size but also because of its methodological standard.[5]

The People's League of Health trial used alternate allocation rather than true randomisation, although the team concerned must have known about Theobald's trial: its medical secretary (W C W Nixon) was affiliated to St Mary Abbots Hospital, where Theobald had conducted his trial. Further, in his report Theobald had foreshadowed the People's League of Health trial by stating that "experiments conducted on these lines would show to what degree the different protective substances are associated with toxaemia symptoms" and that he published the results "in the hope that further experiments on a larger scale will be conducted elsewhere."

We can only speculate why the People's League of Health team did not adopt Theobald's idea of implementing true randomisation; feasibility could be one reason. Perhaps someone knows the relation between these trials and their conduct.

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Memories of why allocation by random sampling numbers was used

Editor—I am one of the last surviving members of the Medical Research Council's streptomycin in tuberculosis trials committee.[1] My recollection is that the committee was aware of the difficulty of avoiding selection bias in allocation to test and control groups in a trial in which blinding was impossible. Because of this we readily accepted the procedure of allocation by random sampling numbers advocated by Bradford Hill and hoped that it would prove practicable.

I was familiar with Bradford Hill's work on the design of clinical trials, both from a course of lectures that he gave in the late 1930s and from reading his book published in 1937.[2] In 1944, during war service in Egypt, I had designed and carried out a double blind placebo controlled study of the effects of sulphonamides in bacillary dysentery; selection bias had been eliminated by the formulation of test and control medications as indistinguishable suspensions, identified by letters.[3] The streptomycin trial could not be blind, either to observers or to patients, and the more complicated method of allocation by random sampling numbers seemed to offer the most promising way of minimising bias.

We welcomed the opportunity to design an objective study of the clinical effects of a promising but unproved antimycobacterial agent in a manner ethically acceptable in the existing circumstances. We realised that it was the decision—for which we had no responsibility but regarded as wise and far sighted—to devote the limited supply then available to such a study that provided this probably unique opportunity.

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Albumin again

Editor—There are only two explanations for the conclusions of the Cochrane review of human albumin administration in critically ill patients—either that albumin was given in excessive amounts or that the commercial processing it undergoes makes it toxic. Several correspondents writing about the review call for expert appraisal of the evidence on which it was based.[1]

As a start I suggest that attention should be directed to the numerous papers

published by the Detroit group, all based on the same 52 patients; five of these studies are included in the review. Lucas et al gave the 27 patients in the albumin group 24% albumin during resuscitation followed by a dose of 150 g/day for five days postoperatively, this dose being "selected to restore albumin levels to normal."[2] Simultaneously, whole blood, fresh frozen plasma, and Ringer-lactate solution were given in amounts greater than to the control group, resulting in a weight gain of about 10 kg in the first 48 hours. This produced the highest relative risk of death (13.93) of all the references quoted.

The conclusions of this group on the perceived malign effects of albumin on the heart, lungs, kidneys, and the coagulation system have been uncritically accepted for over 20 years. They have been quoted by a former director of the Scottish National Blood Transfusion Service[3] and endorsed in the most recent American textbook of perioperative transfusion medicine,[4] as well as having been included in the evidence of the Cochrane review.

In a recent review Margarson and Soni mention the possible toxicity of commercially produced albumin due to aluminium and other metals,[5] and this issue needs to be investigated.

Were I to need a massive transfusion I would happily receive 5% albumin in volumes no greater than the plasma removed from the red cells transfused. Should I be given 24% albumin to maintain "normal" plasma albumin concentrations I might, like Chalmers,[1] think of suing. On the other hand, I might be dead.

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Randomised trials useful to find best methods of enhancing clinical practice

Editor—Although we are flattered that Keirse devoted his whole editorial to our study on the use of educational visits to enhance the use of systematic reviews, we wish to correct some errors.[1 2] Tossing a coin is not inherently a biased method of randomisation, but any open allocation method may lead to selection bias.[3] In our cluster trial we randomly assigned 25 hospitals that had already been recruited to either an educational visit or to a control group, and we blinded data collectors to allocation and outreach visitors to the clinical practices designated as markers. Allocation concealment in such a study is superfluous.

Keirse analysed denominators retrospectively to detect differential data completeness. This analysis is not valid as it ignores the clustering. Excluding the use of steroids, data were obtained for 97% and 95% of the target numbers in the intervention and control groups respectively. Further, follow up data were collected blind to the allocation of the unit which prevented bias.

Keirse states that "22 of the 25 units had a rate of use of ventouse extraction at baseline that was either at or outside the 95% confidence interval for the average." We find this a strange criticism as there is no expectation that observations will lie within the confidence interval. The confidence interval expresses a range of uncertainty for the pooled rate and conveys no information about variation among units.

Keirse comments that 30 cases per unit do not provide an adequate snapshot of clinical practice. A larger sample size per unit would have helped to reduce random variation between and within centres but was not feasible. Our interest was the uptake of Cochrane evidence reflected by the four clinical practices designated as markers. We studied 4508 patients, 92 per unit at baseline and another 88 at follow up. Each audit represented two weeks of clinical practice per unit or one unit year of observation at baseline and a further unit year at follow up.

Finally, Keirse states that the reviews whose impact we studied were published years earlier and that practitioners with any interest would have looked up the results. Keirse himself later correctly states that "perhaps it is too simplistic to expect that merely exposing practitioners to evidence will change practice."[4] Our goal was to promote the interest of lead practitioners in evidence, so we did not distribute review results or dictate which evidence was useful nor how to use it. We agree with Keirse that the best methods for enhancing clinical practice are far from clear, but conclude that rigorous, randomised trials like ours are necessary to explore this issue; one which is important to all healthcare systems.

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Waveforms are needed to interpret figures shown by pulse oximeters

Editor—Spencer and Stringer showed a picture in Minerva of an Ohmeda pulse oximeter with the probe attached to its own connecting cable; the screen showed two figures, 100 representing percentage oxygen saturation and 41 representing pulse rate.[1] They are right to point out the dangers of taking these figures at face value, but the pulse oximeter shown should also display a pulse waveform. Their picture contains no such waveform and thus the two figures are meaningless.

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Unifactorial models are not appropriate for multifactorial disease

Editor—Berger recently discussed the ethical problems of selling Icelandic pedigrees so that genes predisposing to common disorders could be patented.[1] The technical problem "will it work" is also of interest. The belief that multifactorial disorders can be analysed by unifactorial methods underlies the ancestral approach of deCODE.

The company claims, with justification, that it has "formidable capabilities in statistical genetics and uses state of the art techniques of statistical analysis. Since deCODE has access to a large collection of families with extensive pedigrees and family history, the company is able to employ a variety of statistical methods to simplify the search for disease genes. This is particularly important given the competitive nature of large scale genetic analysis."

However, little is said of what these techniques are, or the basis for the statement that "300 000 genotypes a month is enough to allow the company to map 12 complex diseases per year."

Whether "map" refers to bases, kilobases, or megabases is not stated. So far almost all "state of the art" techniques in use for common disorders are based on unifactorial assumptions and have a poor track record. This "flat earth" navigation of the genome, so successful in Mendelian genetics, is inappropriate for the greater distances between gene and body, and the even greater distances between gene and mind, in common causes of common disorders.

Breast cancer is often quoted as a success, but the two Mendelian factors found are not relevant to the common form.

Confidence in deCODE is hardly increased by the advantages Iceland is said to offer. These are stated to include predominantly Viking descent, inbreeding, and major "bottlenecks." Icelanders have a large proportion, possibly a majority, of Celtic genes and are not inbred: the "bottlenecks" were not smaller than the bottom of the bottle, the founding population.

Iceland is ideal for "deep mining" rare disorders, but common disorders require "surface mining" and large pedigrees have little to offer. It was largely the impossibility of such pedigrees being both confidential and informative that led the ethical committee of the Icelandic Medical Council to state: "The committee is completely opposed to the present bill and will advise Icelandic physicians not to participate in the setting up of the database."

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1 Berger A. Private company wins rights to Icelandic gene database. *BMJ* 1999;318:11. (2 January.)

Opposition to the Icelandic database is based on false information

Editor—Duncan states that the legislation on the health database passed by Iceland's parliament last December would allow a private company to link its medical records with genealogical and genetic data.[1]

This statement is false. Personally identifiable data cannot be linked to encrypted medical data in the central database. The legislation simply forbids such use and it is made impossible through ecryption.

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1 Duncan N. World Medical Association opposes Icelandic gene database. *BMJ* 1999;318:1096. (24 April.)

Public policy and mental health legislation should be reconsidered

Editor—Eastman's discussion of the Fallon inquiry into the personality disorder unit at Ashworth high security hospital identifies the dangers for psychiatric practice inherent in public policy in the United Kingdom.[1] We have proposed that mental health legislation should be viewed in a radically new light, separating interventions aimed at treating people in their own best interests who (because of mental incapacity) are unable to take treatment decisions for themselves from interventions aimed at promoting the safety of the public.[2]

Interventions aimed at treating people in their own best interests, but not those aimed at promoting the safety of the public, can be ethically justified on paternalistic grounds. Most violent acts are committed by people who are not mentally ill. Psychiatrists can advise the courts about the presence of mental illness, its prognosis, and appropriate treatment. The evidence base for this advice is strongest for psychotic disorders and weakest for personality disorders. Psychiatrists may infer links between offending behaviour and mental disorder. Judgment about the impact of mental disorder on the degree of responsibility the offender holds for an offence are a matter for the courts.

If society is moving towards the (illusory) goal of eliminating risk it is surely a matter for legislators to delineate the actions to be taken and for the courts to enforce them. We have argued that decisions about the management of people identified as dangerous should come before the courts in a framework of generic dangerousness legislation. Detention for dangerousness, if it is the wish of society, should not apply only to those labelled mentally ill; this is discriminatory and is morally unjustifiable. Only after a decision is made to exclude someone from society on the grounds of dangerousness should the issue of disposal be addressed. Probation officers, social workers, clinical psychologists, and psychiatrists could offer evidence to the courts, but disposal would remain a judicial decision subject to rules of evidence, appeal, due process, and review. Determining whether there is an illness to be treated should come after the decision to detain, not before.

All dangerous people, mentally ill or not, would be treated equally. Innovative psychosocial interventions for dangerous people with personality disorders are urgently required but need not occur exclusively within a psychiatric framework. It is inappropriate to label such people as mentally disordered so that the Mental Health Act can be used as a surreptitious form of preventive detention.

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1 Eastman N. Who should take responsibility for antisocial personality disorder? *BMJ* 1999;318:206-7. (23 January.)
2 Szmukler G, Holloway F. The Mental Health Act is now a harmful anachronism. *Psychiatr Bull* 1998;22:662-5.

Public health psychiatry and crime prevention

Preventive detention of mentally ill people is already widespread

Editor—Eastman's editorial brought the debate about dangerousness and mental disorder to a wider audience.[1] Unfortunately, he failed to point out that the preventive detention of those with untreatable mental disorders is already widely practised in England. Under the Mental Health Act (1983) people with mental illness or severe mental impairment can be detained indefinitely in hospital regardless of response to treatment and on grounds of risk to self as well as others. Secure and open psychiatric hospitals are full of such patients.

If Eastman was concerned that possible new legislation might challenge both the "civil liberties of the unconvicted and those designated untreatable" then surely this concern should extend to the current legislation affecting people with a mental illness or mental impairment. Many psychiatrists find it convenient to make a strong distinction between personality disorder (a largely social condition) and mental illness or impairment (a wholly medical one) and hence view them from different ethical standpoints. Unfortunately, modern neurobiology does not make such a clear distinction.[2] It seems paradoxical that statistically less dangerous mentally ill people are subject to easier and more widespread detention than the more dangerous people with personality disorder.

There is little moral, medical, or scientific distinction between people with mental illness (that is, Asperger's syndrome) and those with personality disorder (that is, schizoid personality disorder). The government's proposals are that doctors' current role as public protectors should be extended to include both groups. This poses new clinical, legal, and practical problems but no new ethical ones.

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1 Eastman N. Public health psychiatry or crime prevention? *BMJ* 1999 318:549-51. (27 February.)
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Psychiatry cannot protect public from people with personality disorder

Editor—Eastman rightly notes that the prospect of indeterminate detention of people who face no criminal charge but are deemed to have "antisocial personality disorder" raises ethical questions for psychiatrists.[1] The growing pressures on them to deliver public protection was perhaps inevitable, given the rise of biopsychomedical paradigms as explanations for the vicissitudes of life in modern Western society.

Psychiatrists have played their part by assuming the authority to explain, categorise, manage, and prognose in situations where well defined disease (arguably their only clearcut remit) was not present. But despite decades of clinical practice and research there is still no compelling case for personality disorder to be regarded as a medical condition. As a psychiatric trainee I was taught that the only solid predictor of someone committing

violence in the future was whether he had done so in the past. This is scarcely a nugget of psychiatric wisdom. The steady rise of violent crime in Britain and elsewhere is not because of undiagnosed "antisocial personality disorder," which is as much the product of social and situational processes as of individual ones.

History shows that when psychiatric models reach out too far into society, the profession comes to look ethically exposed. In 19th century America, slaves who ran away from their masters were deemed to have a mental illness called drapetomania,[2] and in recent times "sluggish schizophrenia" was held to explain and discount the opinions of political dissidents in the Soviet Union. When is the medicalisation of social control legitimate? If psychiatry is to be realistic and ethical, it must publicly admit that it cannot protect the British public from the majority of acts of violence since these are committed by people whom its disease models and thus treatments do not capture.

This admission questions even current remits. On the one hand, it may be unfair to blame consultant psychiatrists when a patient with "personality disorder" kills someone. On the other hand, psychiatrists might have to relinquish that part of their power, status, and salary which they currently claim in relation to their responsibility for such people.

The real arena is sociomoral and political. The withering of extended family networks, the entrenching of systemic underemployment, the diverging economic fortunes of "haves" and "have nots" are all fraying the social fabric, the degree of connectedness of which is the major anticrime variable.

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1 Eastman N. Public health psychiatry or crime prevention. *BMJ* 1999;318:549-51. (27 February).
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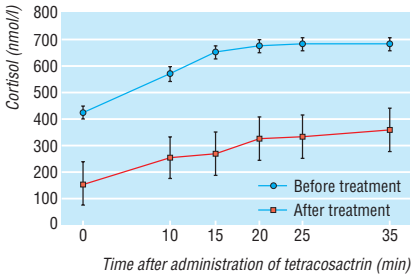
Cushing's syndrome induced by betamethasone nose drops

In rhinological disease betamethasone should be regarded as systemic corticosteroid

EDITOR—We agree with Findlay et al that the few case reports of Cushing's syndrome due to nasal betamethasone drops in children may represent the tip of the iceberg.[1] With colleagues we have performed a prospective study in nine adults with nasal polyposis treated with betamethasone drops for six weeks; we assessed the hypothalamo-pituitary-adrenal axis using a low dose (1 µg) tetracosactrin stimulation test, which may detect more subtle impairment of endogenous cortisol production than the standard test (250 µg).[2] We found that all patients had significantly depressed cortisol concentrations when tetracosactrin was given after betamethasone treatment (figure; $P < 0.0001$, analysis of variance for repeated measures).[3]



Result of low dose tetracosactrin stimulation test before and after six weeks' treatment with betamethasone nose drops

Gallagher and Mackay have suggested that in many cases patients tend to overcomply with treatment with nasal drops owing largely to difficulties in using the droplet dispenser.[4] The perceived benefit of betamethasone over other topical nasal steroids is that its intranasal distribution is superior (because it is in drop form) to that achieved with aqueous sprays.[5]

We endorse the view that in rhinological disease betamethasone should be regarded as a systemic corticosteroid and caution should be exercised.

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1 Findlay CA, MacDonald JF, Geddes N, Donaldson MDC. Childhood Cushing's syndrome induced by betamethasone nose drops, and repeat prescriptions. *BMJ* 1998;317:739-40. (12 September.)
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Children taking intranasal corticosteroids should be monitored for growth retardation

EDITOR—Findlay et al report two paediatric cases of iatrogenic Cushing's syndrome associated with exogenous administration of intranasal corticosteroids.[1] These cases clearly show the potential of "locally active" corticosteroids to cause serious systemic effects. This problem is not, however, limited to betamethasone, nor is it solely the consequence of high doses or exceptionally prolonged administration of this particular corticosteroid.

Reports to the adverse event reporting system of the US Food and Drug Administration have shown that intranasal corticosteroids given by metered dose devices are associated with systemic steroid effects, including Cushing's syndrome and growth suppression. Reports in the peer reviewed literature,[2] as well as unpublished data,[3] indicate that intranasal corticosteroids taken without interruption at the currently recommended doses may significantly reduce growth velocity in children. After a review of these and additional data a joint meeting of the pulmonary-allergy drug and endocrine-metabolic drug advisory committees in July 1998 voted to recommend that the precautions section of the label for all intranasal (and oral inhaled) corticosteroids be amended to reflect these products' potential to inhibit growth in children.

All doctors should be aware of this, particularly as intranasal beclomethasone dipropionate is available without prescription in the United Kingdom. Many patients who are prescribed intranasal corticosteroids for allergic rhinitis also receive orally inhaled corticosteroids for asthma. The additive effects of these drugs[4] and their potential impact on growth velocity are of particular concern.

Growth retardation could serve as an early warning of the systemic effects of corticosteroids, before Cushing's syndrome can be diagnosed. Consequently, to reduce the risk of these untoward side effects, the Food and Drug Administration is recommending that the current label be amended to advise health practitioners that height and weight should be measured regularly in children receiving these drugs. Such measurements offer a rapid, sensitive, and inexpensive screen for detecting decreases in growth velocity and thereby may prevent other systemic adverse effects; they may also help in the development of strategies to reduce dosing.

Data regarding the lowest effective dose of any intranasal or inhaled corticosteroid are scarce. Equally rare are well controlled studies comparing the relative growth effects of different corticosteroids.

It is therefore premature to consider one corticosteroid over another as a means of diminishing this potential problem. Corticosteroids are a valuable therapeutic option in both allergic rhinitis and asthma. Intranasal and oral inhaled products provide a breakthrough in minimising the systemic effects of this class of agents, but the benefits that they offer should be balanced against the complications they might induce.

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1 Findlay CA, MacDonald JF, Geddes N, Donaldson MDC. Childhood Cushing's syndrome induced by betamethasone nose drops, and repeat prescriptions. *BMJ* 1998;317:739-40. (12 September.)
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Learning difficulties may complicate the issue

EDITOR—Findlay et al highlight the dangers of intranasal corticosteroids.[1] We have also recently seen two cases of iatrogenic Cushing's disease associated with betamethasone nasal drops. The first was in an 11 year old boy with Down's syndrome who presented with growth arrest and excessive weight gain. Investigations showed compensated hypothyroidism and normal growth hormone secretion but a suppressed morning cortisol concentration of <28 nmol/l. The second child was a 5 year old boy with non-specific learning difficulties, who presented with voracious appetite, weight gain, and aggressive behaviour. On examination he was obese (body mass index 25.9 kg/m^2) but did not have cushingoid features. A random cortisol concentration was <28 nmol/l. In both children adrenocorticotrophic hormone was suppressed and the plasma cortisol concentration failed to increase after administration of tetracosactrin.

Although prolonged treatment may increase the risks of adverse effects (the first child had been taking betamethasone for three years), the second child had been receiving treatment for less than two months. It is interesting that one of the two children reported on by Findlay et al had Down's syndrome. Children with the syndrome are predisposed to nasal obstruction and rhinorrhoea as a result of their abnormal craniofacial anatomy[2] and may consequently be more likely to receive intranasal steroids. Furthermore, their short stature and tendency to obesity militates against early recognition of excess glucocorticoid exposure.

Both our children had learning difficulties, which added to the difficulty of giving betamethasone drops and may have resulted in overdosage. When intranasal steroids are indicated, giving less potent steroids by metered aerosol should be considered.

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1 Findlay CA, Macdonald JF, Wallace AM, Geddes N, Donaldson MDC. Childhood Cushing's syndrome induced by betamethasone nose drops, and repeat prescriptions. *BMJ* 1998;317:739-401. (12 September.)
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Does the fly matter in trout fishing?

Study broke hallowed tradition among fly fishers

EDITOR—The authors of the CRACKPOT study in evidence based trout fishing are to be congratulated on a study protocol that broke the hallowed tradition of competitiveness and individualism among fly fishers.[1] However, the study's design omitted two major considerations: the time scale used and the character of the respondents.

Firstly, within what random periods did the 125 angling hours take place within the 3696 (5 months $\times$ 24) available to them in the season? The relative values of a Gold Ribbed Hare's Ear and a Cinnamon Sedge, if transposed between a May morning and a September dusk, could give very different results. Secondly, the artificially reared Kennet trout in what is mainly a "put and take" fishery will have had little exposure in their nursery to natural examples of ephemeroptera on which replicas are based. Selection from CRACKPOT's limited trial range will have had relatively little significance to trout conducting their own early examination of human piscatorial behaviour.

Should the group wish to extend their trial on a multiriver basis, I can offer better Test material nearby—based on evidence from 15 flies accepted, often randomly, by some 1200 trout over 20 years.

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1 Britton BJ, Grimley Evans J, Potter JM. Does the fly matter? The CRACKPOT study in evidence based trout fishing. *BMJ* 1998;317:1678-80. (19-26 December.)

Trout in trout fisheries in New England have different interests

EDITOR—In the interest of science the members of the Society for Piscatory Ludics and Animated Snarled-line Hilarium ("SPLASH") have reviewed the fishing logs of our dozen members in order to ascertain the performance characteristics, over the past three years, of the flies in the CRACKPOT study[1] on certain waters of New England. These waters include the Battenkill (in both Vermont and New York States), the Mettowee in Vermont, and the Housatonic in Connecticut. Fishing log data are subject to errors of the order of plus or minus 10% owing to Scotch stains on the logs and the known mendacity of the reporting fisherman.

The logs point to a clear advantage on New England waters when the Parachute Adams is used, followed closely by the Gold Ribbed Hare's Ear. Some standards of deviation away are the other flies of the CRACKPOT protocol, including the Silver (or Cinnamon) Sedge—which was repeatedly refused by local trout until they were informed that the American term for sedge is midge, after which takes improved. SPLASH data show that the Black Gnat fares no better on New England waters than it did on the River Kennet, with one angler reporting brown trout spitting it out derisively.

Certain North American flies outperformed the CRACKPOT protocol. Attractors such as the Royal Wulff scored high in the log analysis, but values must be discounted to reflect the fact that some members use only this fly. The CRACKPOT protocol did not include any Caddis, a major North American pattern. Its success rate is affected by (*a*) the frequency of caddis hatches on New England streams; (*b*) the frequent use of caddis patterns, regardless of the actual hatch; and (*c*) the curmudgeon correlative, which shows the high incidence of American anglers aged over 60 to fish one of a variety of patterns in a single lie until either a trout is landed or hell freezes over.

SPLASH is seeking federal funding for its own study of dry fly performance in comparison with the performance of other types of trout lures and bait. It has been conjectured that the Parachute Adams outperforms corn kernels on a treble hook, but a scientific inquiry is warranted. Our query: did government grants support the authors' drinks cabinet or did lengthy and convoluted explanations of deviations in the home budget have to be made to the wives of the CRACKPOT scientists?

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Authors' reply

EDITOR—We are pleased that the CRACKPOT study should have raised issues of such fundamental scientific importance. The trial took place in May and June, and we agree with Alment that results might not be applicable to September. We also accept that early life experience may have behavioural implications for trout as for humans but doubt if studies among the worldly wise denizens of the Test would have any especial validity. Kennet trout are only caught once (or not, as the case may be).

We can assure our colleagues in SPLASH that, far from receiving government grants, our convivial investigators will have made a substantial contribution to government funds. Furthermore, participation was with the full knowledge and painfully negotiated consent of spouses. We look forward to the results of the projected SPLASH investigation, but comparability with CRACKPOT may be difficult to establish. We suspect that our sedges are not in fact their midges; rather, their caddises are our sedges while our midges are gnats, except when our gnats are something else.

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