Adolescent development

Advice in ABC of adolescence is potentially misleading

Editor—Christie and Viner say that delayed puberty in boys can be quite distressing but is almost always a normal variant. They say that boys aged 15 or over with a testicular volume of 4 ml or more can be reassured that puberty is beginning and, by inference, do not require referral to a specialist. This advice is potentially misleading.

For all that it is a variant of normality, constitutional delay in growth and puberty can have adverse psychosocial and skeletal consequences.¹ To deny an apubertal teenager the opportunity to choose low dose androgen treatment until he is into his 16th year would be unusual by present standards.

Neither does a family history of pubertal delay necessarily support a diagnosis of hypogonadotrophic hypogonadism. Moreover, a history of cryptorchidism (especially if bilateral) or anosmia should prompt an even earlier referral. Neither does a history of pubertal delay necessarily support a diagnosis of constitutional delay in growth and puberty, given the high prevalence of constitutional delay in growth and puberty among first degree relatives of patients with hypogonadotropic hypogonadism.

A recurring theme in the personal stories posted on the www.Kallmanns.org website by men with irreversible hypogonadotropic hypogonadism and therefore by no means necessarily indicates that puberty is beginning. Many boys with hypogonadotropic hypogonadism start puberty but fail to progress beyond the early stages.¹ Moreover, a history of cryptorchidism (especially if bilateral) or anosmia should prompt an even earlier referral.¹

Our advice is appropriate for boys who present to general practitioners. The absence of any signs of puberty, or lack of further progression through puberty over the next six months should, of course, be viewed with suspicion and merit referral to a paediatric endocrinologist for full investigation, including consideration of conditions such as hypogonadotropic hypogonadism.

Quinton thinks that even the normal variant of constitutional delay in growth and puberty can have adverse psychosocial consequences.¹ However, newer larger studies have shown that boys who are small or whose adolescence is delayed are not psychologically disadvantaged.² Rather than overtreating numbers of normal boys, we focus on improving the communication skills of general practitioners in discussing issues such as pubertal timing with young people.

Russell Viner consultant endocrinologist University College London Hospitals NHS Foundation Trust and Great Ormond Street Hospital NHS Trust, London WIT 3AA rivner@ich.ucl.ac.uk

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Cognitive behaviour therapy for adolescents with chronic fatigue syndrome

Data are insufficient and conclusion inappropriate

Editor—I have concerns about the design and interpretation of the study reported by Stulmeneier et al on cognitive behaviour therapy for adolescents with chronic fatigue syndrome.¹ The trial arms were not matched for the number of contacts with healthcare professionals. Experience from larger and more carefully controlled randomised interventional trials of patients with chronic fatigue syndrome has clearly shown that short term improvement in symptoms is related directly to the maintenance of regular contacts with healthcare professionals rather than the therapeutic effect of the intervention itself and consequently, the improvement is not sustained once the contact is lost.

The authors did not offer patients in their waiting list the opportunity to meet therapists regularly for five months but without having cognitive behaviour therapy. Few follow up data on patients in the intervention arm show that the specific treatment benefit was carried forward without regular contacts with the therapists. A cautious approach is essential in inferring direct benefit from cognitive behaviour therapy in the intervention arm (as opposed to short term benefit from close contact with therapists). The level of activity in some of their participants whom the authors considered to be passive remained unclear.

In their summary points the authors claim that cognitive behaviour therapy was effective by challenging patients’ belief that activity aggravated symptoms. Epidemiological data, however, confirm that fatigue made worse by exercise is a characteristic feature of adolescents at risk of chronic fatigue syndrome.¹ Encouraging activity in disabled patients is entirely different from challenging an accepted feature of the disease. A rhetorical approach towards a physically and emotionally challenging condition does not help recovery and only encourages therapeutic failure.

Abhijit Chaudhuri senior lecturer in clinical neurosciences University of Glasgow, Institute of Neurological Sciences, Glasgow G51 1TF ac54p@udcf.gla.ac.uk

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importing the United States and around the world. In the context of these increases, we are surprised that methods of care that might prevent caesarean delivery have not been pursued more aggressively.

Caesarean delivery is strongly correlated to the age of the mother, parity, and increasing gestational age within the term period of pregnancy.1 If caesarean delivery is an adverse outcome worthy of prevention, if risk factors for caesarean delivery can be identified, and if a latent period exists between the identification of risk and the development of situations requiring caesarean delivery then perhaps a preventive approach—encouraging patients with risk factors to enter labour before their risk can become disease—could lower caesarean delivery rates safely.

Our working group recently described the use of risk driven, prestopclagandin assisted induction of labour, and this intervention was associated with a rate of caesarean delivery of only 4%. While Declercq et al think that research should be done to elucidate whether the risks of primary caesarean delivery in cases of no indicated risk will be offset by associated benefits, we hope that an equal amount of time and effort will be spent on developing and testing methods that might safely prevent, or lower, rates of caesarean delivery performed for this and the other more traditional indications.

James M Nicholson assistant professor jenmni.colson@uphs.upenn.edu Lisa C Kellar first year fellow Peter F Cronholm clinic instructor Department of Family Practice and Community Medicine, 2 Gates, Hospital of the University of Pennsylvania, 3400 Spruce Street, Philadelphia, PA 19104, USA

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How to prevent caesarean deliveries deserves more study

Editor—Declercq et al bring to light “no indicated risk” as a new classification of caesarean delivery.1 Like other classes of caesarean delivery, annual rates of caesarean sections with no indicated risk have been increasing in the United States and around the world. In the context of these increases, we are surprised that methods of care that might prevent caesarean delivery have not been pursued more aggressively.

Caesarean delivery is strongly correlated to the age of the mother, parity, and increasing gestational age within the term period of pregnancy. If caesarean delivery is an adverse outcome worthy of prevention, if risk factors for caesarean delivery can be identified, and if a latent period exists between the identification of risk and the development of situations requiring caesarean delivery then perhaps a preventive approach—encouraging patients with risk factors to enter labour before their risk can become disease—could lower caesarean delivery rates safely.

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James M Nicholson assistant professor jenmni.colson@uphs.upenn.edu Lisa C Kellar first year fellow Peter F Cronholm clinic instructor Department of Family Practice and Community Medicine, 2 Gates, Hospital of the University of Pennsylvania, 3400 Spruce Street, Philadelphia, PA 19104, USA

Competing interests: None declared.


Clomipramine and neuroleptic malignant syndrome

Letter on adverse reactions to psychotropic drugs continues to confuse

Editor—Haddow et al describe a severe adverse drug reaction but create an oxymoron in describing clomipramine induced “neuroleptic malignant syndrome.”

Clomipramine is not a neuroleptic and therefore by definition cannot cause this syndrome (any more than it can cause anti-convulsant hypersensitivity syndrome). The description is consistent with serotonin toxicity, a well described adverse reaction to serotonergic antidepressants. In attempting to describe a new adverse drug reaction, Haddow et al have focused on non-specific clinical features that are present in many drug induced neuropsychiatric syndromes.2 Clomipramine, a potent serotonin reuptake inhibitor, has been associated with hyperthermia and was more correctly labelled as a serotonin toxicity.3 Muscle rigidity and raised muscle enzyme activities also occur in severe serotonin toxicity.

Neuroleptic malignant syndrome is an idiosyncratic reaction to therapeutic doses of neuroleptic agents. A pragmatic clinical
description of the syndrome includes four primary features: autonomic lability, hyperthermia (pyrexia) without other cause, extrapyramidal syndrome (cog-wheel or lead pipe rigidity), and encephalopathy. Despite superficial clinical similarities between neuroleptic malignant syndrome and serotonin syndrome, they are usually easily differentiated on the basis of careful neurological examination. Neuroleptic malignant syndrome is associated with lead pipe rigidity, bradykinesia, and other extrapyramidal features. Conversely, in serotonin syndrome there is hyperkinesia, hyperreflexia, and clonus.

Descriptions of adverse reactions to psychotropic drugs need detailed clinical descriptions of neuromuscular, central, and autonomic features. Using ambiguous or non-specific criteria to label adverse reactions as a particular syndrome while ignoring the pharmacology of the implicated drug may lead to false associations between particular drugs and clinical syndromes and to inappropriate treatment.

Authors’ reply

EDITOR—Clomipramine is not a neuroleptic and cannot be weighed against lack of alternatives for many diseases

Risks of gene therapy should be weighed against lack of alternatives for many diseases

Levinson and Sternbach and referenced in our article.[1,2] We described in this patient an earlier diagnosed episode of serotonin syndrome, and no clinical evidence of rigidity was found on that occasion. In view of the action at dopamine sites of clomipramine, and the statement in the BNF from the BMA and the Royal Pharmaceutical Society of Great Britain, we would continue to support our diagnosis of neuroleptic malignant syndrome in this informative case.

Alison Haddow consultnat in old age psychiatry Royal Cornhill Hospital, Aberdeen AB25 2ZH alison.haddow@grampian.scot.nhs.uk

Martin Wilson clinical lecturer Department of Medicine for the Elderly, University of Aberdeen, Aberdeen AB25 2ZD

Competing interests: None declared.

1 Haddow AM, Harris D, Wilson M, Logie H. Clomipramine induced neuroleptic malignant syndrome and pyrexia of unknown origin. BNF 2004;142:153-5 (4 December.)

Artwork of gene therapy

Editors—Devereaux et al discussed the need for expertise based randomised controlled trials for surgical procedures.[3]

Need for expertise based randomised controlled trials

Expertise based design has shortfalls

Editor—Kimmelman provided a comprehensive discussion about the risks and ethics of gene therapy.[4] We certainly cannot predict the future, but the risks should be weighed against the complete lack of alternative options for many of the diseases discussed.

The two cases of T cell leukaemia in the X-linked severe combined immunodeficiency gene therapy trial are presented as typical of new untested strategies with the potential, such as recombinant adeno-associated virus, is much less likely to be mutagenic.

The risks of gene therapy must be weighed carefully against the risks and efficacy of existing treatment. Conventional treatments such as organ transplantation, which are no longer considered experimental, are associated with substantial morbidity and mortality. The difficult balance is to steer a path between the ethical application of new untested strategies with the potential to improve health care, and a position of caution. As with conventional medicines, the risks and ethics of gene therapy should probably be reflected in this light.

Robert E MacLaren MRCPG research fellow Robin RA. professor of human molecular genetics Division of Molecular Therapy, Institute of Ophthalmology, University College London, London EC1V 9EL

Adrian J Thrasier professor of paediatric immunology MRC Clinical Research Centre, UCL, London WC1N IEH

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Artwork of gene therapy
Letters

both arms in proportions reflective of the population that will perform the operations. Academics can analyse the “expertise” subgroup, while the rest of us can look at the overall results to determine how an operation will really perform.

Eric Lim specialist registrar
Papworth Hospital, Papworth Everard, Cambridge CB3 8SR eric.lim@cvet.net

Competing interests: None declared.

Surgical research shares many similarities with psychotherapy research

Editor—Of course the expertise based randomized trial, mooted for surgical procedures by Devereaux et al., is the norm in psychotherapy research when comparing two psychotherapies. A similar debate on the interpretation of such trials occurred in the psychotherapy literature.

Research in surgery and psychotherapy share other similarities beyond having to account for practitioner expertise. There is the issue of blindness—hard to achieve for practitioners with experience, together with “communicators,” and not only by people who studied communication skills who have never had to tell anybody that they have cancer and are dying, or let a family know that a patient has died. The impact of this is greater than most people can imagine, and I think poor communication on those subjects often reflects the inability of the doctor to deal with his or her own feelings.

The same goes for communicating with colleagues. In my hospital, emergency departments are now filmed in major trauma cases, and the people on the floor are actually the ones being filmed. Evaluation is then done by the surgeons, together with a psychologist.

Communication skills are essential, but not at the expense of medical students’ pre-clinical and clinical curriculum. The target groups should therefore be senior house officers and specialist registrars.

Eric T Walbeehm specialist registrar plastic surgery Rotterdam, 3022 KC, Netherlands erikwalbeehm@mac.com

Competing interests: None declared.

Old docs and new tricks

Seasoned doctors may be better than young doctors at some things

Editor—Spurgeon reports that the doctors’ standards of care drop with years in practice.

When I began clinical practice in the late 1980s I thought that one key to being a “good doc” was keeping up with the latest drugs and technologies. I was disillusioned by the debates around the introduction of non-steroidal anti-inflammatory drug to be withdrawn. I then saw many new drugs get pulled from the market (rofecoxib is not the first and certainly not the last) and various medical fads come and go. Evidence based medicine appropriately shed light on the poor evidence available to support most things that physicians do.

Armed with this keener analytical approach, I came to realise that most claims of benefit are greatly exaggerated compared with absolute incremental changes and that most patients are not like trial subjects. Although an intervention might benefit a population, it is much less certain that it will benefit the patient who sits before me. I suspect that seasoned doctors are better than their junior colleagues at some things, and worse at others. Maybe the ability to see the big picture, diagnostically and therapeutically, is enhanced by experience. Meanwhile the emphasis on the newest treatment detail might wane. Perhaps that is a reason why I have conflicting opinions about whether doctors get better with time.

Louis B Jacques physician 918 Barrancata Cove Lane, Annapolis, MD 21401, USA JacquesNL@georgetown.edu

Competing interests: None declared.

Efficiency is important

Editor—In British general practice, where everyday demand exceeds capacity, the efficient general practitioner is king. That is one thing that experience should bring. If all general practitioners followed every guideline the system would collapse, and although a few patients would have exemplary care, many would have no care at all as they would just not get seen because they would find the wait intolerable. Perhaps this is what happens now in secondary care, where care delivered is often very good but access is less and less.

Academic establishment. Many indications for treatment are immediately met with contraindications. Experience allows general practitioners to cut back on too much excess investigation and treatment while still striving to meet the guidelines.

Protecting the patient from the iatrogenic harm of excess health care used to be a core skill of the general practitioner. Is this being taken away from us as well?

A system that fails to value the soft end points and often efficient and effective care that experience brings will have to restructure to meet the demand and that inevitably will lead to a hugely expanded system with resource implications. I am not disputing the findings of the paper reported by Spurgeon, that the standard of care may drop with years spent in practice, but the immediate common sense logic of the hypothesis and conclusions make me advise to proceed with caution. Being a doctor is already a difficult job. Being advised that all your thoughtful patient experience has actually made you a worse doctor is demotivating.

Perhaps experienced doctors and patients would have a different set of criteria about what good care is?

Graeme M Mackenzie general practitioner Whitehaven CA28 7RG graeme.mackenzie@gp-a82041.nhs.uk

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