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Retinal haemorrhages in falciparum malaria

SIR,—Kaur and Taylor, in their otherwise extensive review of retinal haemorrhages in children, omitted arguably the most common cause in the world—falciparum malaria.[1]

Retinal haemorrhages are present on admission in 6–8% of children with cerebral malaria[2 3] with haemorrhages developing in a further 4% of children after treatment (personal observation). Their incidence in uncomplicated malaria has not been established. In adults haemorrhages are associated with more severe disease, as manifest by higher parasitaemias, schizontaemia, anaemia, and increased mortality.[4]

The haemorrhages are often multiple and bilateral. Most are intraretinal, either flame shaped or dot and blot, often developing white centres (Roth's spots) with time. Some are subretinal.[4]

The pathogenesis of the haemorrhages is undetermined. Although they are associated with the development of anaemia in adults with cerebral malaria they are present early in the disease when haemoglobin concentration is relatively high. Intracranial hypertension has been documented in children with cerebral malaria,[2] but there was no correlation between opening lumbar puncture pressure and haemorrhages in this study or a larger adult series.[4] Raised central venous pressure secondary to convulsions may be a cause, but haemorrhages can develop in the absence of seizures. The pathognomic histopathological feature of cerebral malaria is the sequestration of parasitised erythrocytes in small vascular beds including the retinal vessels. We have documented the appearence of haemorrhages at around the time of sequestration on several occasions. Recently it has been suggested that the phenomenon of 'rosetting' of uninfected cells around the parasitised cells plays a part in the pathogenesis of cerebral malaria,[5] and it is possible that the lodging of these agglutinates in the retinal vessels leads to haemorrhages. Haemorrhages were not associated with thrombocytopenia or disseminated coagulation in adults.[4]

Whatever the mechanism, falciparum malaria probably causes, at a conservative estimate, a quarter of a million new cases of retinal haemorrhage a year in children, and as such is worthy of a mention.

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Establishment of working definitions in nocturnal enuresis

SIR,—The recent paper by Dr Butler highlights the need for consistent use of nomenclature when reporting studies of nocturnal enuresis.[1] However there are several points worthy of comment. Why include only those wetting more than 50% of nights during the baseline when this will exclude many enuretics equally in need of help who he admits are 'more difficult to treat'. Furthermore, by selecting only the wettest patients from your baseline period you risk the phenomenon of 'regression towards the mean' biasing your results towards subsequent improvement irrespective of treatment.

The working definitions proposed by Dr Butler would provide only limited information on the effects of drug treatments for enuresis. The application of these definitions would satisfactorily highlight the generally low rates of 'initial arrest' of enuresis and the high subsequent relapse rate,[2] but they would fail to describe the lesser degrees of improvement that many children achieve while taking desmopressin or tricyclics. Although the gold standard for treatment is a 'cure', many fail to achieve this with conditioning therapy and for these children the temporary improvement that drugs may effect, such as an increase in the number of dry nights or a reduction in the size of the 'wet patch', are perceived as worth while.

It is important that these benefits are not overlooked when considering drug treatments for nocturnal enuresis.

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1 Butler RJ. Establishment of working definitions in nocturnal enuresis. *Arch Dis Child* 1991;66: 267–71.
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Dr Butler comments:

Dr Evans's comments regarding my article on working definitions in nocturnal enuresis[1] raise some interesting issues, which are predominantly concerned with the model's applicability to groups of children (for example, those who have infrequent bed-wetting accidents) and methods of treatment (for example, medication) not originally the prime focus of the initial survey.

In an attempt to establish some consistent definitions of nocturnal enuresis, which Dr Evans agrees are badly needed, I embarked on a survey of published reports of conditioning methods, given that these can be regarded as 'easily the most successful specific treatment available'.[2] The method of arriving at the proposed definitions is contained within the article and they were discussed at length at the National Enuresis Research Steering Group, the body which orginally invited me to pursue this work. The suggested baseline inclusion criteria of '50% or more wet nights in a two week period' was offered as a means of encouraging homogeneity of samples in future studies of treatment effectiveness. My intention was clearly not to detract from studies of children who wet infrequently, who as Dr Evans suggests are a very interesting and deserving population. Rather I am concerned that where such a population are studied, for reasons of clarity, the authors might be encouraged to state the degree of severity of wetting. Indeed, I believe the article stated as much.

I would argue that the proposed definitions of initial success, drop out, relapse, etc, although derived from studies on conditioning methods, are equally applicable to assessing the effectiveness of other interventions be they medication, diet, hypnosis or whatever, as they outline, reasonably unambiguously, the criteria to be met.

Dr Evans stresses the absence of measures of improvement for those children who failed to meet the initial success criteria. I would agree that monitoring of progress is essential, whatever the treatment interventions, and indeed measures of improvement such as size of wet patch, time of accident, and so on have been outlined in detail elsewhere.[3] Given such measures, however, the objective either in clinical terms or research methodology must remain the achievement of an initial success criteria.

Dr Evan's final point regarding the probability of regression to the mean is clearly one variable, among many others, that would be controlled for within an appropriate experimental design. However as the regression to mean phenomena tends to describe changes on improvement measures rather than explain complete remission, it further emphasises the importance of establishing criteria for initial success as advocated in the article.

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