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Bamboozled by cBNF

On my drive into work a few weeks ago, BBC Radio 4's *Today* programme announced with some fanfare the publication of the first formulary specifically for children; the *Children's BNF*. As a user of *Medicines for Children (MfC)* for several years this surprised me. There were interviews with experts and a well argued case for the expertise and resources of the *BNF* being used to provide regular updated editions for all medical professionals working with children.

A week or two later it arrived on the wards in familiar *BNF* format with additional helpful comments on the management of common paediatric problems. In A&E this week, after seeing another 18 month old with viral exacerbation of asthma, I attempted to look up the dose of nebulised terbutaline in the *cBNF*. After a frustrating failure I went back to the *Medicines for Children*.

I then conducted a small and very unscientific study ($n = 8$) of paediatric SHOs, middle grades, and nurses to see how long it would take to look up the dose of nebulised terbutaline (commonly used this time of year) for an 18 month old with exacerbation of asthma in the ward's battered 1999 edition of *MfC* and the new *cBNF*. For the *MfC* the average time taken was 18 seconds (range 12–75 seconds). For the *cBNF* only one out of eight was able to find the dose (in 75 seconds) within the two minute time limit. The dosage in the *cBNF* is not on any page number listed in its index, and for those who wish to try the Terbutaline Test the answer's at the bottom of this letter.

The new *cBNF* is a muddy mix of formulary and clinical handbook, and does neither well. The *MfC* was a shining example of clarity and ease of use. Surely an excellent example of "If it ain't broke, don't fix it".

Answer: *cBNF*, p. 157, para 10.

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doi: 10.1136/adc.2005.090464

Competing interests: none declared

Human herpesviruses-6 and -7 and neurological morbidity

We have just become aware of your paragraph in *Atoms*¹ which commented on our accompanying paper, "Human herpesviruses-6 and -7 each cause significant neurological morbidity in Britain and Ireland" in the June 2005 issue of *Archives of Disease in Childhood*.²

Unfortunately, these editorial comments show a complete lack of understanding and misrepresent the findings in our paper.

The study did not set out to determine the frequency of serious neurological disease after HHV-6 and -7 infection and makes absolutely clear in the introduction that primary infection with these viruses is usually silent or sometimes results only in the mild childhood disease, exanthem subitum/roseola infantum. What the work did seek to find, again made plain in the introduction and discussion, was how much of serious neurological disease in children 2 months to 3 years old was caused by these two viruses. Rather than being a case series, our prospective study covered an entire population (that of Britain and Ireland).

In the event, the results have shown for the first time that in the British Isles population surveyed, an unsuspected 17% of cases arose from primary infection by these agents and, equally important, that HHV-7 was a hitherto unrecognised equal contributor to the total burden of such disease.

It is perhaps worth mentioning that your journal's anonymous reviewer of the manuscript for this paper characterised the work as "a landmark study" and when the paper appeared the *BMJ*, picked it out for highlighting and favourable comment.³

Under the circumstances, revision or retraction of your misleading appraisal is the least you can do to make amends so that your readers can understand our findings in the proper context.

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on behalf of N J Andrews, C M Verity,
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Competing interests: none declared

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Is Chandipura virus an emerging human pathogen?

Chandipura virus (CHPV), initially thought to be an orphan virus, was later reported to cause sporadic cases of fever with arthralgia,¹ Reye's syndrome,² and epidemic coma. Epidemic coma was reported as epidemic brain attack of childhood (EBAC) (supported by clinical features, normal CSF in all cases, neuroimaging, and response to treatment)^{3–5} or Chandipura encephalitis (supported by virus isolation, identification by electron microscopy, immunofluorescence, and PCR).^{6–9}

CHPV is ubiquitous in the Indian subcontinent (at least since 1955),¹ Sri Lanka,¹⁰ and Africa (Nigeria, Senegal).^{11,12} Human cases have only been reported from India. CHPV can infect many other mammalian species. The high prevalence of specific antibodies and viral RNA in the population

of India combine to obscure any potential role of this virus in paediatric illnesses, and the matter remains unresolved.¹³ Chandipura virus has been employed for several years in academic virology laboratories as a substitute for the animal pathogen, vesicular stomatitis virus, in research on interferon, for assay of retroviruses by pseudotype formation, and as a vehicle for antigen presentation. There have been no adverse consequences.^{14,15}

Isolation and detection of CHPV, serological status, and presence of viral antigen in brain biopsy by immunofluorescence assay, while providing reasonable evidence of an association between CHPV and the outbreak,¹⁶ fulfil neither the Bradford Hill criteria nor modified Koch's postulates.^{3,17} Since there is histopathological evidence of an inflammatory reaction in the brains of mice,¹⁶ but not in humans, it could be a passenger virus, a concomitant virus, or a pathogenic virus in humans.³

In an outbreak of EBAC, clinicians critically argued against the diagnosis of encephalitis and a pathogenic role of CHPV since the linkage between CHPV and EBAC was not proved.^{3,17} In subsequent papers,^{6,9,18,19} virologists avoided arguing against the ischaemia hypothesis or defending the diagnosis of encephalitis or the aetiological role of CHPV by ignoring that report, and did not even reference the articles.^{3–5,17,21}

Evidence of atypical measles encephalitis in an identical epidemic by the same authors²⁰ was subsequently believed to be a laboratory contamination with measles vaccine virus.²¹ Evidence from multiple studies from multiple laboratories is necessary before accepting CHPV as a human pathogen (as has been done for SARS).

Evidence of the presence of the virus, its genome, or antigen or antigen-antibody complex in the middle cerebral artery in at least some cases would confirm the aetiological role of the CHPV in EBAC.

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doi: 10.1136/adc.2005.074708

Competing interests: none declared

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