LETTERS TO THE EDITOR

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Sweat chloride and conductivity 1

**Editor,—**As a principal author of the sweat testing document published by National Committee for Clinical Laboratory Standards (NCCLS) and consultant to the Cystic Fibrosis Foundation (CF) (USA), I write to address an inaccuracy in the article by Heeley et al. The authors misrepresent the NCCLS document on the role of conductivity analysis. Nowhere does the NCCLS document refer to the current conductivity methods described in the paper as unreliable; it does, however, accept the fact that older conductivity methods are subject to evaporation error. The NCCLS document goes on to state that the CFF has approved the use of newer conductivity analysers for the screening of cystic fibrosis (CF) at community hospitals, using a decision level of 50 mmol/l.

The reliability of many of the accepted fact that chloride determinations directly reflect the genetic mutation of the disease. Conductivity is a property of all the charged species in a sample—for example, sodium, potassium, chloride, lactate, bicarbonate, etc. As the authors point out, chloride provides greater discrimination than sweat sodium—that is, less overlap between diagnostic categories. It would seem logical then, that combining sodium with chloride in a conductivity measurement would effectively cancel out the discrimination advantage of chloride alone. Referring to the data presented in table 2, there were twice as many patients with equivocal conductivity concentrations as with chloride (albeit a very limited sample size). Additionally, there exists a paucity of data in the scientific literature comparing conductivity and chloride values in CF and non-CF individuals. Even the scientists publishing such research support the conclusion that conductivity is appropriate for initial screening and chloride for confirmatory diagnosis.

Heeley et al’s article attempts to provide relevant data, however it is most unfortunate that the authors failed to include in their analysis a linear regression plot of chloride versus conductivity, along with a bias plot of the data so that the reader could assess the correlation. Most readers need to be published comparing conductivity with chloride, particularly in patients with results in the equivocal range, before the conclusion can be made that sweat conductivity is as effective as chloride measurement for the diagnosis of CF.

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Dr Heeley et al respond

**Editor,—**As the principal author of the NCCLS guideline on sweat testing methodology, Dr LeGrys should be better informed of its content. It includes the clear statement that when sweat test results are obtained by conductivity measurement “the patient should be referred for quantitative sweat electrolyte testing”. In our paper we refer to this statement as implying that sweat conductivity measurement should be regarded as “unrelatable for diagnostic purposes”. This surely cannot be conceived as misrepresenting the NCCLS position, as claimed by Dr LeGrys. Although the NCCLS does, by reference, attribute this advice to Cystic Fibrosis Foundation (CFF) (USA) policy, by including it in their guideline without comment or qualification, the NCCLS authors are actively promoting its use.

The medical politics of the USA do not concern us, but rather the question as to whether there is any scientific evidence underpinning this advice which the NCCLS uphold. The result of our study suggests there is none.

Dr LeGrys quotes research findings which support the conclusion that sweat conductivity measurement is appropriate only for initial screening purposes. We contend that there is no data presented in this otherwise excellent paper which provide scientific justification for that conclusion.

Dr LeGrys is of the opinion that the conclusion we draw from our own study should have been supported by appropriate linear regression and bias plots of the data. The *Archives*’ professional statistical adviser reviewing our manuscript, which included such data analysis, thought otherwise and requested us to remove it.

It is rather ironic that Dr LeGrys should now be pleading for more studies to be carried out to resolve the issue of the diagnostic equivalence of indirect and direct sweat electrolyte measurement, focusing on patients who produce results which are equivocal. Considering the relative rarity of such patients in general paediatric practice, if the problem revolves around these cases, why did the NCCLS guideline not state this in the first place? In reality, the final diagnosis of cystic fibrosis in these cases is likely to be resolved by the results of investigations other than the sweat test.

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Sweat chloride and conductivity 2

**Editor,—**As I understand the Scientific Method, a statement purporting to be factual, either in a scientific article or in a discussion with peers, must be supported by cited evidence that may be publicly examined for its scientific veracity.

The paper by Heeley et al provides data to illustrate the equivalence of conductivity and chloride in cystic fibrosis (CF) diagnosis, and therefore corroborates the findings of an earlier clinical trial by Hammond et al. Further, a statistical comparison of the extensive published data from Shwachman et al with the conductivity data of Hammond shows that the two are of equal discriminatory power in CF diagnosis.

Despite this evidence, Dr LeGrys has authored a document that contains a number of assertions on this subject and on other aspects of sweat testing, that are not supported by any published results of original work of which I am aware. No clinical trial data exist which show that conductivity should only be used as a screen, that it is in any way inferior to chloride as a reliable diagnostic discriminator, or that conductivity readings of 50 mmol/l are positive for CF. Dr LeGrys’ call for more studies on this matter may be seen as an evasion of the true issue. I suggest that the time has come, albeit belatedly, for her to substantiate her case, not with opinions, but by providing proper citations for relevant experimentally obtained data to support her contentions in the said document.

In a separate article Dr LeGrys refers to conductivity as a “qualitative” assay, appearing to infer that it is less reliable than chloride analysis. The term “quantitative”, used in the pad-absorption method merely indicates that...
Dipstrip examination for urinary tract infection

EDITOR,—We read with interest the letter by Thayyil-Sudhan and Gupta reporting their study on the role of dipsticks in the detection of urinary tract infection in children.1 We believe that this is a very important subject and therefore most care should be undertaken routinely. Several standard textbooks of neonatology recommend repeating the lumbar puncture routinely in the course of newborn bacterial meningitis, to ensure that “meningitis” continues to improve. This recommendation is based on past practice, and current evidence in favour or against repeating the lumbar puncture in newborn bacterial meningitis is not clearly established.

However, we have observed that day to day clinical practice appears to have changed and fewer repeat lumbar punctures are being done. To investigate this we performed a simple questionnaire survey across the north of our hospital of sending urine for culture. We wanted to see if a change in practice to urine culture being done only if nitrites or leukocyte esterase were positive would be effective in reducing the number of urine cultures.

The inclusion criteria for Sharief and colleague’s study1 was a clinical suspicion of urinary tract infection, when urine cultures were sent and dipstick testing was done. We found that urinary tract infection could easily be missed if urine cultures are used. If nitrites or leukocyte esterase are positive. Surprisingly, the results of both our study and theirs are similar: sensitivity was 34.4% v 20.0% and specificity was 90.7% v 99.2% in our study and Sharief and colleague’s study. Negative predictive value was 92.4% in our study and 96.7% in Sharief’s study. Only the interpretation of the results is different.

A test with such a low sensitivity cannot be recommended as a screening test to exclude urinary tract infection. Urinary tract infection may result in irreversible renal damage in infants and therefore most care should be given to the detection of this infection in this age group. Unfortunately it is the group where sensitivity of dipstick testing is the lowest (20%). I agree with Sharief and colleague’s study1 that because of its high negative predictive value, dipstick testing may have some role as a screening test for urinary tract infection in situations where the incidence is very low. Positive nitrites have a high specificity for urinary tract infections, which is the basis of our suggestion that if nitrites are positive, especially in a febrile infant, empirical treatment with antibiotics may be considered until the result of urine culture is obtained. However, it should not be the whole criterion for diagnosis of this infection.

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Should repeat lumbar punctures be routinely done in neonates with bacterial meningitis? Results of a survey into clinical practice

EDITOR.—Neonatal meningitis remains a very important cause of morbidity and mortality, with 30% death or handicap rate reported in a recent study.2 In common with other clinical situations, the evidence base for some of the management recommendations for good clinical practice is hard to find. One particular aspect of the management of neonatal bacterial meningitis is whether or not a repeat lumbar puncture should be undertaken routinely. Several standard textbooks of neonatology recommend repeating the lumbar puncture routinely in the course of neonatal bacterial meningitis, to ensure that “meningitis” continues to improve. This recommendation is based on past practice, and current evidence in favour or against repeating the lumbar puncture in neonatal meningitis is not clearly established.

We have observed that day to day clinical practice appears to have changed and fewer repeat lumbar punctures are being done. To investigate this we performed a simple questionnaire survey across the north of
We need the full picture on both smacking and vaccinations

EDITOR—Dr Elliman is noted for his careful methodological analysis of vaccination studies,1 but is not so careful in his recent analysis of physical punishment.2 The American Academy of Pediatrics’s co-sponsored scientific consensus conference on corporal punishment used a more scientific approach than the Elliman-Lynch summary. First, it carefully defined spanking as a subset of corporal punishment. Second, it incorporated a range of scientifically validated perspectives into summary statements, that were more balanced than the Elliman-Lynch perspective. Third, it solicited the first systematic review of child outcomes of non-abusive or customary physical punishment by parents,3 which was recently updated.4 Both reviews concluded that non-abusive smacking had consistently beneficial child outcomes in the most causally conclusive studies—for example, randomised trials. Both non-compliance and fighting decreased in 2–6 year olds after non-abusive smacking was used to back up milder disciplinary tactics, such as reasoning or time out. Causal evidence of detrimental effects of customary physical punishment was less conclusive and limited to overly frequent smacking—for example, three times weekly for 6–9 year olds. In head-to-head comparisons, the effects of non-abusive or customary smacking rarely compared unfavourably with any disciplinary alternative, whereas its effects were significantly better than six alternative disciplinary tactics, mostly in 2–6 year olds. My updated review considered all 92 studies included in the unpublished 1999 Ger-shoff review cited by Elliman and Lynch. Most (76) of her studies were excluded from my review for reasons that Elliman would use to discount vaccination studies—for example, inappropriate measures, cross sectional designs. Ellison and Lynch also presented a one sided summary of Swedish statistics since their 1979 smacking ban. Additional information on this issue and other related issues can be found at http://people.biola.edu/ faculty/paup/1. The issues are complex, requiring the careful analysis given to concerns about vaccination.

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Oral steroids and inflammatory markers in asthma

EDITOR—We thank Dr Grigg for his interest in our work.1 We agree that the asthma attacks may have resolved spontaneously in some cases, which was precisely why we stated that the markers fell in association with steroid therapy, and not necessarily causality. Nevertheless, the statistical analysis suggests that the chances this occurred at random are extremely low.

We agree that corticosteroids do not inhibit, except at very high concentrations, degranulation of the eosinophils induced by incubation with opsonised particles, such as Sepharose beads in vitro.2 However, there is overwhelming evidence that cytokines such as IL-5 prime eosinophils for increased release of granule proteins in this situation,3 4 and that they inhibit cytokine-mediated prolongation of eosinophil survival.5 These observations, coupled with the abundant evidence that corticosteroids reduce the expression of eosinophil-active cytokines, such as IL-5, provide a convincing chain of evidence linking the clinical use of corticosteroids with reduced release of eosinophil granule proteins in vivo.

With regard to the controls in this study the ratio of atopic to non-atopic asthmatics was 4:1 and of atopic to non-atopic controls was 3:1. These differences are retested using chi-squared testing. Whilst we agree that more controls might have strengthened our conclusions, nonetheless the evidence of suppressed inflammation and that a selective approach to clinically adequate course of prednisolone, as shown by the elevated levels of IL-5 and sCD25, remains strong.

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Table 1

Table 2

Oral steroids and inflammatory markers in asthma

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BOOK REVIEW


Progress in the management of disease in the newborn has carried with it a recognition of the substantial risk of injury to the immature nervous system. The aspiration to localise the substantial risk of injury to the immature newborn has carried with it a recognition of that risk.

The evaluation of the newborn nervous system was originally based upon concepts learnt from adult neurology. The baby was seen as demonstrating little or no cortical or cerebellar activity and the study of primary reflexes predominated. The approach of adult neurology, with emphasis on localisation of the lesion, becomes less applicable in the younger child. In the newborn period, focal insults to the brain will often give rise to generalised disturbances and, contrarily, generalised disturbances may show focal deviations. Recognition of these phenomena has led to a progression from the concept of a localisation based neurology to one which sees the infant displaying a neurological/behavioural repertoire. Over the past several decades Saint Anne Dargassies, Prechtl, Amiel Tison, Brazelton, Dubowitz, and others have, through meticulous study, done much to illuminate this area. Through these studies, awareness of the importance of the behavioural state of the baby, as well as the more intricate neurological items has evolved.

A second problem in this area, particularly in relation to research studies, has been the development of a systematic newborn neurological examination which is reliable and repeatable. This has been the subject of the two editions of this work. The first, published in 1981, gave a detailed, easily understood and applied system for the neonatal neurological examination. The current edition brings that work up to date. New material is presented, refinement of the scheme has occurred, and the examination is described. Items which were less discriminatory of pathology from the 1981 version have been withdrawn and, following the work of Prechtl, more emphasis is placed on the analysis of general movements. There is a further post neonatal to two year old infant neurological examination proforma presented briefly at the end of the text.

The text is essentially a manual on the application of this neurological examination scheme. It is easy to follow and the segments of the examination are presented clearly with excellent photographs and line drawings of each manoeuvre. There is also a useful addendum (“cautionary tales”) to each section of the examination, giving guidance on possible pitfalls and sources of error. There is a lot of very useful information on the variations in findings in term and preterm infants, and particularly the changes in the neurological features of preterm infants as they grow towards term. There follows a section on the development of an optimality score from the observed items of the assessment. This section deals with the results of a survey of 224 normal term infants. In this study each item of the scheme was plotted, and centile values (and thereby optimality scores) were computed. This provides quantification of the assessment, a sense of the range of findings to be expected, and can be useful in correlating lesions observed on neuro imaging with clinical findings. Chapter six deals with the scheme in relation to findings in infants with recognised brain lesions.

The book is not designed to be a text of neonatal neurology and readers looking for discussion of neurological disease states will be disappointed. As a description of a comprehensive and easily applied system of neonatal neurological examination the new edition succeeds admirably.

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