LETTERS TO
THE EDITOR

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The editors will decide, as before, whether to also publish it in a future paper issue.

Sweat chloride and conductivity 1

**EDITOIR**, 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 (CCF) (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 reflect the widely accepted fact that some older conductivity methods are subject to restate the widely accepted fact that some older conductivity methods are subject to unreliable readings of 50 mmol/l. This decision level is supported by the data presented in the Heeley article. The data presented in the article concerning equivocal patients also support the US reference interval for sweat chloride as normal below 40 mmol/l. Patients with chloride values greater than 40 mmol/l should be further evaluated.

The reluctance of many to accept the use of sweat conductivity in place of sweat chloride for confirming a diagnosis of CF is based on the 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 studies 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

**EDITOIR**, 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 “unreliable 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 (CCF) (USA) policy, by including in their guideline without comment or qualification, the NCCLS authors are actively promoting it.

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 NCCLS’ 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 guidelines 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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Data from: www.archdischild.com
Dipstick 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. We believe that this is a very important subject and wish to comment on the report and their conclusions in the light of our published study.¹

We note that as 188 urine samples were not sent for culture, it is not possible to determine the number of true and false negative dipstick tests (if any). Without these data, calculation of sensitivity and specificity of dipstick testing becomes impossible.² Because of the above we believe that the data presented are not secondary to a flawed experimental design. Consequently, the statement of the authors that urinary tract infection in children cannot be excluded by a negative nitrite or leukocyte esterase reaction is difficult to justify. Furthermore, there is no information to indicate whether children who were being treated with antibiotics at or immediately before admission were included in the study. If this is the case, the possibility of false negative culture results cannot be excluded and this will add further bias to the results. No data are provided for the number of infants included in the study. It has been reported that negative dipstick tests have a higher false negative rate than positive results in situations of urinary frequency because decreased bladder incubation time diminishes in vivo bacterial multiplication.³ We are not told about the percentage of the samples, which were collected by pads, as opposed to those collected by bladder catheterization if this information is available. This possibility, all urine was sent for laboratory analysis. The laboratory was unaware of the results of the dipstick tests until the end of the study. Analysis of our data showed that the combination of negative dipstick tests for nitrite and leukocyte esterase or blood gave a negative predictive value for urinary tract infection of 96.9%, with a specificity of 98.7%. The figures for infants were 96.7% and 99.2%, respectively. A positive nitrite and/or leukocyte esterase had a positive predictive value of 60% and a sensitivity of 54.6%, compared with 50% and 20.0% respectively in infants. In our series we found that there were four false negative and six false positive nitrite tests.

The dipstick tests are most likely to be useful as a screening test to exclude urinary tract infection in children but may be less suitable for infants. They should not be used to diagnose urinary tract infection in infants because negative dipstick results cannot be relied on to exclude urinary tract infection in this group. There is a high false negative rate of 26% and a false positive rate of 30% using dipstick tests in infants. Positive nitrite and leukocyte esterase tests should therefore be regarded as a presumptive diagnosis of urinary tract infection in children. The diagnostic sensitivity of a positive dipstick test is 80% and specificity is 90% in children. The rate of false positive results is 10%.

Dr Thayyil-Sudhan and Dr Gupta report the following:

Our study involved a selected group of children who were at an increased risk of having urinary tract infection. The inclusion criteria were the presence of any of the following: firstly, clinical suspicion of urinary tract infection; secondly, history of previous urinary tract infections or renal anomalies; thirdly, children needing antibiotics (urine culture was sent before starting antibiotics); and finally, any of the dipstick tests (nitrites, protein, leukocyte esterase, or blood) being abnormal.

Out of the 500 children admitted to our hospital during the study period, only 312 met the above criteria and were included in the study. Urine culture was done for all these children, which reflects the local practice at 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 colleagues' study 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 culture is used, whether 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's study respectively. The 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, this is an age group where sensitivity of dipstick testing is the lowest (20%). We agree with Sharief and colleagues' study 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 was 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 diagnosis for diagnosis of the 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.¹ 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 ² 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 available.

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

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Table 1 Results of the questionnaire survey

<table>
<thead>
<tr>
<th>Question: Do you routinely repeat LP in proven neonatal meningitis?</th>
<th>&lt;10 years experience</th>
<th>&gt;10 years experience</th>
<th>DGH</th>
<th>Tertiary centres</th>
</tr>
</thead>
<tbody>
<tr>
<td>Routinely repeat LP</td>
<td>3.6%</td>
<td>14.6%</td>
<td>5.5%</td>
<td>12.8%</td>
</tr>
<tr>
<td>Do not routinely repeat LP</td>
<td>38.5%</td>
<td>43.2%</td>
<td>47.7%</td>
<td>33.9%</td>
</tr>
</tbody>
</table>

DGH, district general hospital; LP, lumbar puncture.

Table 2 Breakdown of those who responded

<table>
<thead>
<tr>
<th>Registrars</th>
<th>Consultants</th>
<th>&lt;10 years experience</th>
<th>&gt;10 years experience</th>
<th>DGH</th>
<th>Tertiary centres</th>
</tr>
</thead>
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<td>47.7%</td>
<td>33.9%</td>
<td>54.1%</td>
</tr>
</tbody>
</table>

LP, lumbar puncture.

EDITOR,—Dr Elliman is noted for his careful evidence to support a change, yet in some neonatal experience (table 2). It is unnecessary trauma—35 (39%) It will not help in deciding the duration of therapy—63 (70%) It is recommended in textbooks—9 (45%)

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We need the full picture on both smacking and vaccinations

EDITOR,—Dr Elliman is noted for his careful methodological analysis of vaccination studies, but is not so careful in his recent analysis of physical punishment.

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, which was recently updated.

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 Gershoff 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/paulp/. The issues are complex, requiring the same 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, degradation of the eosinophils induced by incubation with opsonised particles, such as Sepharose beads in vitro.1 However, there is overwhelming evidence that cytokines such as IL-5 prime eosinophils for increased release of granule proteins in this situation,1,4 and that they inhibit cytokine-mediated prolongation of eosinophil survival.1 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 asthma was 4:1 and of atopic to non-atopic controls was 3:1. These differences are significant by chi-squared testing. Whilst we agree that more controls might have strengthened our conclusions, nonetheless the evidence of suppressed inflammation and that a significant proportion of patients achieve clinically adequate course of prednisolone, as shown by the elevated levels of IL-5 and sCD25, remains strong.

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1 Grigg J. Oral steroids and inflammatory markers in asthma [Rapid Response]. Arch Dis Child. 16 April 2000. http://adc.bmj.com/cgi/letters/archdischild/84/2/134

172 (100%) surveys posted
112 (63%) responded
3 (1.5%) were invalid (incompletely filled)

Answer: NO, 89 (82%) do not routinely repeat LP and will only repeat if clinically indicated, because:
It will not help in deciding the duration of therapy—63 (70%)
Clinical improvement is more important—61 (68%)
It is unnecessary trauma—35 (39%)
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 the importance of the behavioural state of the baby, as well as the more discriminating neurological items that has evolved.

A second problem in this area, particularly in relation to research studies, has been the difficulty of correlating lesions observed on neuro imaging with clinical findings. Chapter six 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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