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 (CFF) (USA), I write to add 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 recognize the widely accepted 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 new conductivity analysers for the screening of cystic fibrosis (CF) at community hospitals, using a decision level 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. Moreover, 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

**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 “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 (CFF) (USA) policy, by including it 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 upholds. 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 factually correct, 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. Furthermore, a statistical comparison of the extensive published sweat chloride data of 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...
LeGrys, in her letter makes the incredible statement that sodium is not as reliable as chloride as a discriminator it would seem “logical” (sic), that because conductivity measures both, the discriminatory advantage of chloride would be cancelled out. The logic of this is difficult to comprehend. Increase in sweat chloride due to functional aberration of the chloride channel must be compensated by increase of one or another of the available cation species—for example, potassium, sodium, or ammonium, in order to satisfy the Law of Equivalent. Such an increase in chloride will therefore be reflected by a proportionate increase in the total electrolyte concentration, which is the basis of urine electrolyte conductivity.

It is regrettable that lack of proper attention to basic scientific principles has persisted in the NCCLS guidelines for sweat testing for a considerable time without comment. Sweat has produced increasing confusion among medical technologists, particularly in the United States. It is sincerely hoped that the author of this document will see fit to amend it appropriately by substituting scientific accuracy for prejudice.

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References


Dr Thayyil-Sudhan and Dr Gupta

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 (nitrates, protein, leukocyte esterase, or blood) being abnormal.

Out of the 500 children admitted to the 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 nitrates or leukocyte esterase were positive would be effective in reducing the number of urine cultures.

The inclusion criteria for Sharief and colleague’s 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 cultures are used, whether if nitrates 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. Positive 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 infec- tion 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, the group where sensitivity of dipstick testing is the lowest (20%). I agree with Sharief and colleague’s study that because of its high negative predictive value, dipstick testing may have some role as a screening tool for urinary tract infection in situations where the incidence is very low. Positive nitrates have a high specificity for urinary tract infections, which was the basis of our suggestion that if nitrates are positive, especially in a febrile infant, empirical treatment with antibiotics may be considered instead of urine culture is obtained. However, it should not be the whole criterion for diagnosis of this infection.

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Letters, Book review

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. 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.

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, calculations of sensitivity and specificity of dipstick testing becomes impossible. Because of the above we believe the data presented are misleading or at best 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. Fur-
smacking and vaccinations


different from that promulgated in the
circumstances day to day clinical practice is
especially when there is little new published
neonatal experience (table 2).

Table 1 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>
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</thead>
<tbody>
<tr>
<td>Routinely repeat LP</td>
<td>3.6%</td>
<td>14.6%</td>
<td>5.5%</td>
<td>12.8%</td>
<td>14.6%</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>
<td>54.1%</td>
</tr>
</tbody>
</table>

DGH, district general hospital; LP, lumbar puncture.

We need the full picture on both
smacking and vaccinations

EDITOR.—Dr Elliman is noted for his careful
methodological analysis of vaccination stud-
ies, but is not so careful in his recent analysis
of physical punishment.1

The American Academy of Pediatrics's
cosponsored scientific consensus conference
on corporal punishment used a more scien-
tific approach than the Elliman-Lynch sum-
mary. First, it carefully defined spanking as a
subset of corporal punishment. Second, it
incorporated a range of scientifically vali-
dated 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 punish-
ment by parents,2 which was recently up-
dated.3

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 con-
lusive 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 stud-
ies 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 infor-
mation on this issue and other related issues
can be found at http://people.biola.edu/ faculty/paulp/. The issues are complex,
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Oral steroids and inflammatory
terators 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 causal-
ity. 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
Seapharose beads in vitro.1 However, there is
overwhelming evidence that eosinophils such
as IL-5 prime eosinophils for increased release of granule proteins in this situation,2 4
and that they inhibit cytokine-mediated pro-
longation of eosinophil survival.2 These
observations, coupled with the abundant evi-
dence that corticosteroids reduce the expres-
sion 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 pro-
teins 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
3:1. These differences are not attributed by
chi-squared testing. Whilst we agree that
more controls might have strengthened our
conclusions, nonetheless the evidence of
suppressed inflammation and a lack of associa-
tion with clinically adequate course of prednisolone, as
shown by the elevated levels of IL-5 and
sCD25, remains strong.

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Regulatory effect of cytokines on eosinophil degranulation.

Arch Dis Child: first published as 10.1136/adc.84.5.450a on 1 May 2001. Downloaded from http://adc.bmj.com/ on June 3, 2022 by guest. Protected by copyright.
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 complexity of skills are constantly changing, the child grows and develops, the range and 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 detailed 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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