Maternal smoking and blood pressure in 7- to 8-year-old offspring

Editor,—Morley et al demonstrate convincingly that the systolic blood pressure of offspring when compared with non-smoking mothers was significantly lower if they were delivered before 33 weeks' gestation but significantly higher if they were born at 33 or more weeks.1 No direct mechanism for this finding is suggested.

Using unbiased methods, we determined the precise relationship between fetal renal number and gestational age, confirming unequivocally that almost half of the total complement of glomeruli is generated during the last few weeks of normal nephrogenesis—this is, between week 32 and 36 of gestation.2 We also documented that type II intrauterine growth retardation, such as is associated with maternal smoking and which was recorded in the >33 weeks' group of Morley's study, results in an irreversible loss of 50% or more of glomeruli in most cases.3 In animals, neonatal unilateral nephrectomy has been shown to result in compensatory glomerular hypertrophy, increasing the filtration area available, but requiring increased glomerular perfusion and, in turn, a raised perfusion pressure.4 The finding of Morley et al, of a difference in the blood pressure of the offspring of smokers related to delivery before or after 33 weeks', may now be explained by hypothesising continued nephrogenesis ex utero between week 33 and 36 in the early delivered group, in contrast to a loss of up to 50% of nephrons in the post 33 week group as a result of continued intrauterine exposure to adverse circumstances. Indeed as infants delivered to smoking mothers before 33 weeks' in this study showed normal birthweight ratios, it is probable that a developmental defect does not exist in this group. However, in the post 33 week group with low birthweight ratios, a glomerular deficit, requiring a compensatory raised blood pressure in later life, seems likely.

It is perhaps important to reiterate that although postnatal weight gain in growth retarded infants may approach the original genetic potential, the 'window of opportunity' nature of nephrogenesis precludes such recovery and compensatory mechanisms may develop with profound effects on morbidity and mortality in later life.

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REFERENCES

LETTERS TO THE EDITOR

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Dr Morley comments:
The data put forward by Hinchliffe, Howard and van Velzen do not entirely explain our findings.
We reported previously that in a cohort born up to 33 weeks of gestation decreasing size at birth was not associated with the rise in later blood pressure reported in population studies5 and hypothesised that the adverse influence of growth retardation on later blood pressure takes place later in gestation.
As a group, babies born preterm do not grow well in the neonatal period and often suffer severe growth retardation. If continued nephrogenesis depends on good nutrition we might expect that the children who grew best or received a nutrient enriched formula should have lower later blood pressures. This was not the case; neonatal ex utero growth failure did not influence later blood pressure.6 Further analyses have shown that in those children born before 33 weeks of gestation the degree of growth failure after delivery did not influence later blood pressure, whether or not they were born growth retarded.
If the cause of higher later blood pressure in children born growth retarded is reduced glomerular numbers, then from our data we could speculate the released as a result of growth retardation only adversely influences glomerular numbers if it occurs in utero and either starts or continues after 33 weeks of gestation.
In the group born after 33 or more weeks of gestation (almost all of whom had birth weights below the 10th centile) we found an adverse influence of maternal smoking on later blood pressure, in contrast to population studies.2 We speculated that maternal smoking is deleterious for later blood pressure only if the fetus is exposed to it late in gestation and in the presence of growth retardation.
It would be interesting to investigate whether smoking in late gestation influence glomerular numbers and whether there is any interaction with growth retardation.


Plasma interleukin-3 and interleukin-4 concentrations in Turkish asthmatic children

Editor,—Asthma comprises a clinical-pathological triad of intermittent and reversible airway obstruction, chronic bronchial inflammation with eosinophils, and bronchial smooth muscle cell hyper-reactivity to bronchoconstrictors, which may be initiated by mast cell activation in response to allergen binding to IgE.1 Multiple, multifunctional cytokines are released as a result of IgE mediated mast cell activation.2 Interleukin (IL)-4 is a potent stimulant for T cell growth and development and acts independently of IL-2 induced T cell proliferation.3 IL-3 is a pleiotropic cytokine that stimulates the proliferation and differentiation of haematopoietic progenitor cells, but also enhances the expression of class II MHC molecules, which play an important part in T cell mediated immune response.4 IL-3 and IL-4 may have significant autocrine effects on the mast cell itself and these cytokines may facilitate IgE production by these cells.5 It is now generally accepted that IL-4, IL-6, and interferon gamma play the main parts in the regulation of human IgE synthesis.6 This concept is based mainly on in vitro data.7 We measured plasma IL-3 and IL-4 concentrations in 20 Turkish children with bronchial asthma, who were diagnosed according to Lawlor and Taskin's criteria.8 There were 13 boys and seven girls ranging in age from 49 months to 14 years, with a mean (SD) age of 8.0 (3.1) years. Twelve patients received prophylaxis with ketotifen, eight with theophylline, and all the patients were given β-adrenergic agonists during acute attacks. None of the patients were receiving immunotherapy. Twenty healthy children with a mean (SD) age of 9.1 (3.2) years were included in the study as a control group.

Mean (SEM) plasma IL-3 and IL-4 concentrations in asthmatic patients and control group

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<th>Asthmatic patients (n=20)</th>
<th>Healthy controls (n=20)</th>
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<tr>
<td>IL-3 (pg/ml)</td>
<td>7.78 (2.49)</td>
<td>ND</td>
</tr>
<tr>
<td>IL-4 (pg/ml)</td>
<td>31.30 (1.64)</td>
<td>ND</td>
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ND: non-detectable. Minimum detectable concentrations were considered non-detectable.

None of the patients had received corticosteroids in the last six months which might block cytokine production. Ketotifen antagonizes mainly IgE induced release of mediators.1 Adrenergic agents and theophylline raise cAMP in the bronchial smooth muscle cells and inhibit contraction.2 Therefore, of the four groups in treated and untreated asthma only ketotifen may have influenced the results. However, no significant difference in plasma IL-3 and IL-4 concentrations was found between the patients receiving ketotifen and theophylline.

Schauer et al have reported an in vivo pre-activation of lymphocytes from asthmatic patients with increased concentrations of IL-4.7 Bruinzeel et al have found that IL-3 and IL-5 are demonstrable in the circulation of asthmatic, but not normal, individuals.8 Schleimer et al have proposed that local release of IL-4 in vivo in allergic diseases may explain the enrichment of eosinophils and basophils observed in asthmatic patients.9 Our data have revealed additional in vivo evidence of increased concentrations and activities of IL-3 and IL-4 in extrinsic asthmatic children.
A judicial comment on temporary brittle bone disease

EDITOR.—A recent reported judgment by Mr Justice Wall1 in the Family Division of the High Court is relevant to the debate on temporary brittle bone disease.2 The case is relevant as it expresses the view that this diagnosis to explain injuries in both child protection and criminal court proceedings is largely due to the work of Paterson.3 In the case reported he was asked how two earlier cases of injuries had been before the court and had been treated in his research data. In one case there had been a criminal conviction and in the other there had been a finding of non-accidental injury by the Wards Humphry Court. It is reported that Paterson replied that both cases were included in his research as proven cases of brittle bone disease. Indeed, when asked how he would log the case before the court (the baby had suffered brain injury and multiple fractures), should the judge make a specific finding of non-accidental injury, he replied that he would still regard the case as being one in which the child had suffered temporary brittle bone disease. In the words of the judge ‘Whilst courts of course accept that there may be cases where there is a divergence between judicial and clinical findings, I regard as worrying in the extreme Dr Paterson’s failure to record in his research material of cases of proven brittle bone disease judicial findings to the contrary. In my judgment this is a factor which must cast the gravest doubts on his findings’.

The judgment also reaffirms that the courtroom is no place to advance untested hypothesis and emphasises the need for expert witnesses to provide independent assistance to the court and not omit to consider facts which detract from their concluded opinion. Attention is also drawn to an earlier judgment by Cazaela,4 also involving brittle bone disease, which points out that a misleading opinion from an expert may well inhibit a full assessment by non-medical advisers, reinforce parental denial, and thereby put a child at risk.

For future cases coming before the High Court there will be awareness of previous judgments relating to evidence on temporary brittle bone disease, however, this may not be so in the Family Division of the Court. As Mr Justice Wall comments: ‘It is not difficult to imagine circumstances in which a non-accidentally abused child might be returned to abusing parents on the false premise that the child has not been abused. That in my judgment is just as much an injustice as a false finding that a parent has injured a child’. During investigation of suspected child abuse, even before legal action is considered, the possibility of temporary brittle bone disease may be raised and threaten to compromise or obstruct protection of a child or therapeutic work with their family. By being aware of and referring others to relevant reports5 paediatricians can help keep the issues in perspective.

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Infant length measurements

EDITOR.—Dr Doul1 and colleagues presented a paper on the reliability of infant length measurements.2 Hoora! Some of us have for many years tried, without much success, to encourage the measurement of infant length. In many studies it is a better measurement of growth than weight and is a stable linear growth measure. Why the unsucces? ‘It’s very difficult to do; it’s unreliable; you need a special apparatus; it’s impractical to do in the field’. It has been shown that none of these concerns is valid,3 but Dr Doul has done so in an up-to-date persuasive way including showing that you do not need two professionals but only one, mothers being excellent holders of their infants’ heads.

For velocity growth in infancy it is an important measure and there are a growing number of reference values available.4

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This comprehensive book covers all aspects of trauma care. It starts with a historical review, discusses the philosophy and organisation of paediatric trauma management, describes the treatment of specific conditions, and looks to the future.

There are 85 contributors (mainly surgeons) three of whom are Australian, all the others being North American. The book was more than six years in gestation and the chief editor himself has to produce a book that reads so fluently.

There are six separate sections. The first covers the history of the subject, the biomechanics of trauma, injury prevention, organisation of services, and developing standards of care. The figures report the agencies involved in prevention and some of the legislative solutions suggested have an American slant. Nevertheless, the principles of aetiology and prevention are universal and well described.

The chapter on trauma care organisation is excellent. Care of the injured starts at the roadside or in the home and continues until tertiary care is reached and provided. The authors write with authority on the improvement in care following the introduction of a team approach to the injured child ‘There is a role... for competition amongst care providers’. The response teams are described. Resuscitation and stabilisation are orthodox and follow advanced paediatric life support and advanced trauma life support (APLS, ATLS) teaching. There are some exceptions: for example, use of a trolley in introducing a chest drain is deplored as dangerous by most of us in emergency care. The radiological evaluation is clear and unexceptional, but our anaesthetic colleagues may balk at the suggested use of ketamine in potentially hypotensive, cerebrally injured children.

In fairness, the author admirers to differences of opinion over this. He is not dogmatic: ‘No singular approach should be considered the only correct approach. Rather a protocol for trauma care that is attuned to the institution’s geographic and urban demographics, the availability of surgical expertise and the physical limitations of the building itself is appropriate’.

Chapters are devoted to trauma scores, protocols, and blood products. There is detailed consideration of specific system injury and then to special situations such as falls, birth injuries, non-accidental trauma, farm and submersion injuries. My surgical colleagues assure me that the operative procedures described are standard. A conservaive approach is taken to urinary tract injuries and liver damage, but a slightly more aggressive approach than ours to splenic injury. A