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Interleukin-1α and soluble interleukin-2 receptor in atopic dermatitis

SIR,—Dr Agata and colleagues reported enhanced interleukin-2 (IL-2) activity in blood mononuclear cells from patients with food sensitive atopic dermatitis following allergen exposure.[1] Soluble interleukin-2 receptor (sIL-2R) is an indirect marker of T cell activation by IL-2 and raised concentrations have previously been described in adults with atopic dermatitis.[2] However, in vitro studies suggest that IL-2 secretion by T helper cells is not only antigen driven but it is also dependent on interleukin-1 (IL-1) expression by cells of the macrophage/monocyte series; IL-1 also upregulates the expression of high affinity receptors for IL-2 on T helper cells type 1.[3] In order to investigate this hypothesis, we measured IL-1α and sIL-2R using an ELISA technique. Twenty three children were assessed: 11 with atopic dermatitis and 12 non-atopic normal controls. The results are shown in the table.

	Controls	*Atopic dermatitis*	*Unpaired t p value*
Mean age (years)	9·2	8·6	NS
Range	4–14	4–16	
IL-1α (pg/ml)	163	369	p<0·02
95% CI	56 to 269	232 to 505	
sIL-2R (U/ml)	189	377	p<0·02
95% CI	75 to 301	262 to 492	

CI=confidence interval.

There was a strong direct correlation between IL-1α and sIL-2R ($r=0·67$, $p<0·001$) which suggests that expression of the two are dependent. While no apparent relationship existed between either cytokine concentration and disease severity using the criteria of Rajka and Langeland[4] or IgE concentrations, our results demonstrate that there is enhanced endogenous secretion of IL-1α, and increased stimulation of IL-2 receptors, in children with atopic dermatitis. These findings suggest that these cytokines may contribute to the inflammatory process in atopic dermatitis and are consistent with the observations of Dr Agata and colleagues.

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Pulse oximetry reference values at high altitude

SIR,—Lozano *et al* in their article on pulse oximetry reference values at high altitude conclude that their reference values could be used for the interpretation of oxygen saturation at high altitude in Bogota and other cities at a similar altitude.[1] However, the authors have failed to take into account potential sources of error.

The fall in arterial oxygen saturation at altitude is due to the fall in barometric pressure rather than the gain in altitude *per se*. There is a corresponding fall in atmospheric oxygen tension (Po_2) with fall in barometric pressure (at 2000 m atmospheric $Po_2=124·9$ mm Hg (16·6 kPa) and at 3000 m $Po_2=110·2$ mm Hg (14·7 kPa)[2]) such that the author's proposed reference ranges are not suitable for use at altitudes other than that of Bogota (2640 m) as even small changes in altitude will alter the availability of atmospheric oxygen and the arterial oxygen saturation.

Furthermore, at a given altitude the barometric pressure changes with local variations in weather and to a greater extent with the season such that in mid-summer the barometric pressure may be 11 mm Hg (1·47 kPa) higher than in winter.[3] Moreover, there is an equatorial bulge in the atmosphere such that the barometric pressure at a given altitude near the equator is higher than at the same altitude nearer the poles by 17 mm Hg (2·27 kPa).[4] These pressure variations will affect the partial pressure of oxygen in the atmosphere. Although of little significance at sea level pressures, these changes in atmospheric Po_2 in the already 'desaturated' infant at altitude may significantly affect arterial saturation.

Taking these observations into account the authors may find that there are both seasonal and latitudinal variations in arterial oxygen saturation along with the changes in barometric pressure such that their proposed reference ranges should be intrepreted with caution in summer and probably not used at all at latitudes or altitudes distant from Bogota.

Before recognition of these changes in barometric pressure with season and latitude the ascent of Everest (8848 m) without supplementary oxygen was thought impossible. In 1978 Messner and Habeler proved the physiologists wrong.[5]

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Randomised trial of nutrition for preterm infants after discharge

SIR,—This interesting study draws attention to a possible need for preterm infants to be fed a slightly higher protein, mineral, and energy-containing milk in the first nine months after birth.[1] However, the authors include detailed tables on feed tolerance, stool number, size and consistency, and skinfold thickness (which show no significant differences between diet groups) yet choose not to present any data on growth of weight, length, and head circumference on which they base their conclusions of a possible advantage for this specially designed formula. It is not enough to say that differences are apparent on visual inspection of the charts. In fact, looking at these it seems to me that if there are any differences at all they take place for length and head circumference only in the first few weeks: after this the curves virtually parallel each other. Weight does fall off in those fed the standard infant formula but only between about 6 and 18 weeks. Growth data have been meticulously collected and the statistical methods explained in detail but without giving information, on velocity or incremental growth, it is difficult to evaluate the findings of the study.

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Drs Lucas, Bishop, and Cole comment:

Professor Davies seeks further information on growth in our study on postdischarge nutrition. The growth data collected at two weekly intervals are shown in our paper graphically (tabulation would have been cumbersome and the graphic data show centile placing). Given the small sample size, as expected, relatively few individual two week measurements showed a significant difference between groups. Nevertheless, in view of the consistently increased weight, length, and head circumference at every two week period up to 9 months' corrected age in the infants fed the fortified diet, we explored whether the overall growth trajectory was different between groups. This is a statistically robust procedure as, unlike the *t* test comparisons of individual two weekly data points, we were taking the entire growth data set for each diet group into account. As growth trajectory is not linear, but curvilinear, growth velocity was calculated from a quadratic fit of the data. The significant differences we reported in length and weight gains between feed groups would be difficult to describe numerically, short of presenting equations for the quadratic curves, and we elected not to. We emphasise, however, that our statistical analyses confirm a clear advantage in weight and length gain ($p<0·005$ and $p<0·01$ respectively) for infants fed the fortified formula. The difference between groups in rate of head growth did not achieve significance, because the early divergence between groups tended to diminish later in the study period. Nevertheless, the head growth issue needs further exploration especially in view of our unpublished analyses that show a trend towards higher gross motor development scores at 9 months in infants fed the fortified

diet; but many more subjects would be required to test these aspects adequately.

We should be very happy to discuss our growth data in greater depth with individual investigators.

Growth patterns after surgery for virilising adrenocortical adenoma

SIR,—We agree with the notion of Salt *et al* in their article on growth patterns after surgery for virilising adrenocortical adenomas that more information is needed on the natural history of growth and pubertal development in these children.[1] We therefore have recently published observations on growth in 10 children aged 0·8 to 11·8 years with hormonally active adrenocortical tumours (nine carcinomas, one adenoma) before and after surgery (excess of androgens 10/10, of glucocorticoids 5/10, of estrogens 1/10).[2] In addition, five of 10 patients had a palpable abdominal tumour at the time of initial presentation. In only one patient increased longitudinal growth alone had initiated the diagnostic workup.

Only two of our patients had a preoperative height SD score >+2. In one patient, an increase in height SD score above baseline was noted simultaneously with the first signs of precocious sexual maturation. However, in five of seven patients followed up postoperatively, in whom removal of the tumour controlled symptoms of hormone excess, height SD score initially declined after surgery. We took this as evidence for catch-down growth, comparable with that in patients with congenital adrenal hyperplasia and delayed initiation of treatment.[3] Although Salt *et al* state that no catch-down growth had occurred in their patients,[1] at least in five of them a period of rapid growth was followed by normalisation of growth velocity and a trend for the bone age to come back in line with the chronological age, similar to our patients. The fact that in most of their patients final height SD score was higher than height SD score at the time of diagnosis is no evidence against postoperative catch-down growth, as at that time the majority of patients were of an age at which most children may not have shifted yet to the definitive centile range that they tend to follow for the remainder of their growth.

Finally, the course of the two patients described by Salt *et al* who had androgen and glucocorticoid excess agrees with our observation that in instances where high concentrations of both hormones affect the growing bone simultaneously, the androgen effect on linear growth and bone maturation appears to dominate. This is different from normal puberty, where hypercortisolism can inhibit longitudinal growth in the presence of physiological concentrations of gonadal steroids.[4]

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Terbutaline sulphate Turbuhaler in severe acute asthma

SIR,—Pedersen *et al* have shown the efficacy of 0·25 mg of terbutaline administered by Turbuhaler (Astra) in acute asthma.[1] We similarly treated 20 patients with a mean age of 9·9 years (range 5–15) who had acute asthma and severe airway flow limitation.[2] They were taking prophylactic drugs (inhaled nedocromil sodium and/or budesonide) and inhaled β_2 agonists before coming to our unit.

Spirometry (Vitalograph) was performed (best out of three) at 0, 30, and 60 minutes before each dose of terbutaline and again at 90 minutes. The patients inhaled 2·5 mg of terbutaline sulphate (five doses of 0·5 mg/2 minutes), followed by a further 2·5 mg and 1 mg (two doses of 0·5 mg/2 minutes) at 0, 30, and 60 minutes. The results, as a percentage of predicted values, are shown in the table. One way analysis of variance of repeated measures and adjacent difference contrasts for pairs showed significant differences ($p<0·05$) between pairs for all but the 60–90 minute pair for $FEF_{25\%-75\%}$.

Results of spirometry

	Time (min)			
	0	30	60	90
FVC	66·4	89·2	96·8	102·7
FEV_1	50·2	72·4	82·3	87·8
PEFR	50·0	70·3	77·7	86·0
$FEF_{25\%-75\%}$	32·5	56·3	67·6	71·7

FVC=forced vital capacity, FEV_1=force expiratory volume in one second, PEFR=peak expiratory flow rate, $FEF_{25\%-75\%}$=force expiratory flow between 25% and 75% of the forced vital capacity.

In two cases, despite clinical improvement, there were no important changes in spirometry even after the administration of 0·5 mg nebulised salbutamol.

Clinically, all patients achieved a normal breathing pattern between the first and third dose without side effects.

In conclusion, the Turbuhaler seems to be effective in severe acute asthma.

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