suggests, as do our data, that responses to 1- α -OHD₃ and 1- α , 25-(OH)₂D₃ are different enough to have important implications in treatment. Although hypercalcaemia remains a serious risk with all vitamin D derivatives the rapid reversal that is possible after 1- α , 25-(OH)₂D₃ treatment makes this agent preferable to calciferol and possibly to 1- α -OHD₃. This is particularly so in patients in whom hypercalcaemia is most likely to be troublesome—for example, those with precarious renal function, or those in whom hypercalcaemia has been previously induced.

This work has been supported by the National Fund for Research into Crippling Diseases. JAK held an MRC clinical research fellowship during part of these studies.

We are grateful to Leo Laboratories for supplies of synthetic 1- α -OHD₃; to Roche Products Ltd for synthetic 1- α , 25-(OH)₂D₃; and to Professor J A Strong and Drs J G G Ledingham, D O Oliver, and R Smith, who allowed us to study patients under their care.

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(Accepted 4 November 1976)

SHORT REPORTS

Colour vision in vitamin A deficiency

Colour blindness is known to occur as a sex-linked genetic trait. A relatively high incidence of colour vision defects has been reported in patients with cirrhosis of liver.¹⁻³ Cruz-Coke postulated a common genetic basis for defective colour vision and cirrhosis,¹ while other workers have suggested that defective colour vision may be secondary to liver disease.² Bronte-Stewart and Foulds observed that in patients with biliary cirrhosis who had impaired dark adaptation and defective colour vision vitamin A treatment produced a significant improvement.³ It was suggested that these defects may be due to associated vitamin A deficiency. Vitamin A deficiency affects rod function with loss of dark adaptation, but little is known about the effect of hypovitaminosis A on cone function. We therefore investigated this point.

Patients, methods and results

Twenty-eight children, aged 4 to 12 years, with clinical signs of vitamin A deficiency were investigated. They showed conjunctival xerosis or Bitot spots, or both. Eighteen also had night blindness. The American Optical Hardy-Rand-Rittler (HRR) pseudoisochromatic plates were used to detect colour vision defects. Venous blood samples were obtained and serum vitamin A was estimated by a trifluoroacetic acid method.⁴ The children were treated with vitamin A 24 000 IU/day for 15 days.

Colour vision was normal in all the children. Serum vitamin A levels ranged from 0.14 to 0.70 μ mol/l (4–20 μ g/100 ml). Sixteen of the 28 children had vitamin A values below 0.35 μ mol/l (10 μ g/100 ml). Two weeks after treatment with vitamin A night blindness and conjunctival xerosis disappeared in all the children, but the Bitot spots persisted in some.

Comment

Vitamin A deficiency is a major nutritional problem among children in many developing countries. The classical manifestations of vitamin A deficiency are night blindness, conjunctival xerosis, and Bitot spots. Severe deficiency of vitamin A, resulting in keratomalacia and total blindness, is seen mostly in preschool children.

It is generally agreed that serum vitamin A levels under 0.70 μ mol/l (20 μ g/100 ml) indicate vitamin A deficiency. In our study only those children who had serum vitamin A concentrations below 0.70 μ mol/l were tested and colour vision was found to be normal in all. Many had night blindness. These results indicate that vitamin A deficiency affects the rod function but not the cone function. Since vitamin A is required for regeneration of the visual pigments of both rods and cones in the retina, it has been postulated that hypovitaminosis A may lead to impaired dark adaptation as well as defective colour vision. Cone pigments, however, synthesise much more rapidly than rhodopsin,⁵ so rod function is the first to be affected in vitamin A deficiency. Possibly cone function may also be affected in severe deficiency, but then it may be difficult to evaluate colour discrimination because of more serious corneal involvement.

Our findings disagree with those of Bronte-Stewart and Foulds.³ They studied two patients with biliary cirrhosis who showed a significant improvement in colour vision six weeks after treatment with

vitamin A. It is possible that hepatic function might also have improved by the time their patients were retested. Other workers have observed that in patients with cirrhosis of the liver the defects in colour vision disappeared after the patients recovered from their decompensated cirrhosis.² Our results show clearly that vitamin A deficiency per se does not affect colour vision. It may be argued that our method of testing colour vision is not sensitive enough to detect minimal changes. But such changes, even if they occur, may not have much practical importance.

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(Accepted 24 September 1976)

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Salty sweat and ichthyosis in Addison's disease

The clinical manifestations of primary chronic adrenocortical insufficiency are well known.¹⁻³ Recently we saw a patient with Addison's disease who had two unusual features—namely, "salty sweat" and ichthyosis. To our knowledge these features have not been reported before.

Case report

A 54-year-old Indian stevedore was admitted to hospital in August 1975 for investigation of suspected Addison's disease. He had noticed increasing darkening of his skin during the past year associated with asthenia and weight loss. He also said that his sweat tasted excessively salty, and he had noticed this at work when sweat dripped down his face. When it dried he sometimes found fine, white particles on his body that tasted like salt. He had also observed that the skin over his legs was dry. He had no salt craving or gastrointestinal symptoms, and there was no history of tuberculosis. His skin was hyperpigmented, particularly over the exposed areas, flexures, and palmar creases. There were irregular areas of hypermelanosis on the tongue gums, and buccal mucosae. Even the nails were black. The skin over his shins was ichthyotic. The blood pressure was 85/55 mm Hg. Nothing further was found on examination.

Investigations showed: haemoglobin 12.8 g/dl; white cell count $11.3 \times 10^9/l$ ($11\ 300/mm^3$), with 15% eosinophils; blood urea 10.3 mmol/l (62 mg/100 ml); blood glucose 5.4 mmol/l (98 mg/100 ml); and serum sodium 129 mmol(mEq)/l, potassium 5.2 mmol(mEq)/l, and chloride 97 mmol(mEq)/l. Chest and abdominal x-ray pictures were normal. Antinuclear factor and thyroid and parietal cell antibodies were absent. The basal plasma cortisol concentration was low and there was no response to prolonged stimulation with tetracosactrin, which confirmed primary adrenocortical failure. Sweat was collected from his back and tested for electrolytes.

Two months after treatment with cortisone acetate and fludrocortisone the patient felt well and had gained weight. The skin over his legs was normal. No local treatment was given for the ichthyosis. Much of the hyperpigmentation was reversible. The sweat test was repeated (see table).

Sweat electrolyte concentrations (mmol/l) before and after corticosteroids

	Before treatment	After treatment
Sodium (normal $51.9 \pm 2SD\ 42.2$)	87.0	18.0
Chloride (normal $29.7 \pm 2SD\ 17.7$)	71.0	3.2
Potassium (normal $7.5 \pm 2SD\ 3.2$)	3.7	16.0

Conversion: SI to traditional units—Sweat electrolytes: 1 mmol/l = 1 mEq/l.

Comment

Clearly the salty sweat and ichthyosis resulted from chronic adrenocortical insufficiency, as both reverted to normal after corticosteroid replacement. Changes in the electrolyte composition of sweat in adrenal disorders are familiar and have been used as an index of adrenocortical function. However, salty sweat in Addison's disease is a remarkable symptom. In this disease the excessive secretion of sodium chloride in sweat is secondary to mineralocorticoid deficiency.

The acquired ichthyosis is more difficult to explain. The hydration of the skin may have been affected by the osmotically more active sweat or by the reduction of dermal blood flow due to chronic hypotension, or by a combination of both. Glucocorticoids may perhaps influence the keratinisation of the epidermis. Ichthyosis also occurs in another endocrine disorder—namely, hypothyroidism.

Salty sweat and ichthyosis may now be regarded as unusual manifestations of Addison's disease.

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(Accepted 24 September 1976)

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Disodium cromoglycate can inhibit virus-induced cytopathic effects in vitro

Disodium cromoglycate is a potent drug used to prevent attacks of bronchial asthma and seasonal rhinitis.^{1,2} It can prevent immune complex-induced exocytosis of histamine granules from mast cells,³ probably by inhibiting calcium influx at the plasma membrane.⁴ It is not known whether the clinical efficacy of the drug lies in this "membrane-stabilising" effect only. A common clinical experience is that exacerbations of asthma are often associated with viral infections of the upper respiratory tract. The possible interference of disodium cromoglycate with virus replication and virus-cell interactions has not been investigated thoroughly.

We report here some findings that may be relevant for planning research on this subject.

Methods and results

Confluent cultures of BS-C-1 cells in Falcon plastic tissue culture flasks or glass tubes were infected with adenovirus 5, echovirus 6, and 7, herpes simplex virus type 1, or Semliki Forest virus in the presence or absence of 10 mg/ml disodium cromoglycate (Lomudal). Replication of the viruses was followed by daily microscopy of the cultures.

Cromoglycate prevented or delayed the appearance of typical cytopathic effects caused by the viruses. The protective effect was dose-dependent in two dimensions, being more pronounced at low multiplicities of infection and undetectable below 1 mg/ml of disodium cromoglycate. Results from a standard infectivity titration of four of the viruses in the presence of 10 mg/ml of disodium cromoglycate are shown in the table. No effect on uninfected cultures was visible in these experiments, but when BS-C-1 cells were passaged several times in the presence of 10 mg/ml of disodium cromoglycate the cells flattened and the rate of cell proliferation slowed down. These effects were fully reversible in 24 hours when the growth medium containing the drug was replaced by normal one.

The drug may not have any direct effect on the viruses, as pretreatment of echovirus 7 virus with 10 mg/ml disodium cromoglycate did not diminish its infectivity. Furthermore, one-step replication curve of Semliki Forest virus in BS-C-1 cells, as studied by plaque assay of virus infectivity, was not changed, despite complete inhibition of the concomitant cytopathic effects in the cultures. On the other hand, agglutination of goose erythrocytes by Semliki Forest virus was inhibited by cromoglycate at concentrations as low as 100 µg/ml. These results suggest that the inhibition of virus-induced cytopathic effects by disodium cromoglycate may be based on preventing the cytolytic effects of the viruses rather than on interfering with the replication of the viruses.

Effect of disodium cromoglycate on infectivity titration of some viruses in BS-C-1 cells*

Virus	Lowest dilution causing typical cytopathic effects	
	Normal medium	With 10 mg/ml disodium cromoglycate
Adenovirus 5†	10^{-4}	$<10^{-1}$
Echovirus 7†	10^{-4}	10^{-1}
Herpes simplex† ..	10^{-4}	10^{-2}
Semliki Forest virus‡ ..	10^{-7}	10^{-3}

*Cell cultures were washed twice with Hanks's balanced salt solution and refed with Eagle's minimal essential medium with or without 10 mg/ml disodium cromoglycate and supplemented with 3% calf serum, 50 µg streptomycin, and 50 U/ml penicillin. Virus dilutions were added and cytopathic effects were recorded after 3 days' incubation at 37°C.

†Recent isolates.

‡A laboratory strain derived from prototype isolate of SFV, kindly provided by Dr L. Kääriäinen.

Comment

The concentrations of disodium cromoglycate required for this cytoprotective effect were about 1000 times those active in "stabilising" mast cell membranes.³ It would therefore be easy to ignore these observations as an unspecific effect completely irrelevant to the clinical action of the drug. Nevertheless, under 5% of a given inhalation dose of DSCG will be absorbed from the lung, while most of the rest will be either trapped by the upper respiratory tract or transported back to the throat by the ciliary epithelium of respiratory tract, swallowed, and secreted in the faeces.⁵ Inhaling several doses of disodium cromoglycate daily, 20 mg each, could result in relatively high concentrations of the highly hydrophilic drug in the thin aqueous film on the laryngopharyngeal mucosa. This might not protect these tissues from viral infections, but by preventing tissue destruction, high concentrations of cromoglycate could diminish local inflammation and thereby effectively alleviate the symptoms of the disease.

We thank Fisons Ltd, Loughborough, UK, for providing the disodium cromoglycate.

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(Accepted 16 November 1976)

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