

British Association of Allergists

The summer meeting of the British Association of Allergists was held at the Department of Pathology, Cambridge University on Saturday, July 1st, 1961.

The subject of the morning session was milk allergy and the meeting opened with a talk by A. M. Barrett, R. R. A. Coombs, Mavis Gunther and W. E. Parish on "Milk hypersensitivity and sudden death in infancy". This was followed by the guest speaker C. Collins-Williams (Canada) on "Cows' milk allergy in infants and children". In the afternoon J. Landon spoke on "The prevention of some side-effects of cortico-steroid therapy" and was followed by H. Morrow Brown who spoke on "Steroid therapy in chronic asthma".

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Milk hypersensitivity and sudden death in infancy

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Part I: The Background

At least 25% of all deaths of infants aged 1-6 months occur sufficiently suddenly to be reported to the Coroner. Typically, an infant about 3 months old is left in its cot apparently well, and is later found dead. Such deaths occur more frequently in males than in females; they are twice as common in the winter as in the summer; often there is a history of a recent cold. These facts suggest that respiratory infection may be the cause of these deaths, and the finding of inflammatory changes in the respiratory tract at autopsy supports this view. On the other hand the inflammatory changes are relatively slight, and not of a kind which suggests a virulent infection; and search for a possible causative bacterium or virus is usually unsuccessful. An alternative possibility is that infants may become sensitized to milk, and that they may then die if they inhale a small amount of food or vomit, which would be more likely to happen if they were suffering from nasal obstruction due to a "cold". Data concerning feeding habits have provided some support for this view: in 44 cases of sudden death in infancy none of the infants were breast fed, whereas of 75 control infants 11 were breast fed. A study of the effects of the introduction of milk into the respiratory tract of sensitized animals therefore seemed worth while.

Part II: Experimental Work

Guinea-pig sensitized to the proteins of cows' milk by intraperitoneal injection show typical anaphylactic shock if milk, in quantities quite innocuous in unsensitized animals, is administered into the larynx. However the syndrome produced by this means is not compatible with that of cot death in infants. Death is violent and agonal, and not quiet and insidious as must be the situation in human cot-death cases.

A completely different picture results if milk is dropped into the larynx of the sensitized guinea-pig while under light anaesthesia to simulate sleep of the human infant.

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Here respiration ceases and death follows – but without any struggle. Also the pathological findings in the lungs are not incompatible with those observed in human cot-death cases. Evidence that many infants are in an “allergic state” with regard to cows’ milk proteins comes from the clinic and from the results of a survey of the antibodies to milk proteins in the sera of normal infants. This antibody level is high in the sera of the majority of cot-death cases. The hypothesis held at present is that the sleeping infant regurgitates stomach contents containing cows’ milk proteins and aspiration of this material into the lungs of the sleeping sensitized infant results in the fatal syndrome seen experimentally in the guinea-pig. Further work is in progress.

References

Gunther, Mavis ; Aschaffenburg, R.; Matthews, R. H.; Parish, W. E. and Coombs, R. R. A.: The level of antibodies to the proteins of cows’ milk in the serum of normal human infants. *Immunology* 3: 296-306 (1960). Parish, W. E.; Barrett, A. M. and Coombs, R. R. A.: Inhalation of cows’ milk by sensitized guinea-pigs in the conscious and anaesthetized state. *Immunology* 3: 307-324 (1960). Parish, W. E.; Barrett, A. M.; Coombs, R. R. A.; Gunther, Mavis and Camps, F. E.: Hypersensitivity to milk and sudden death in infancy. *Lancet* 2: 1106-1110 (1960).

Cows’ milk allergy in infants and children

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Cows’ milk allergy is a fairly common and extremely important form of allergy seen in infants and children. Its signs and symptoms are very protean and may involve many body systems, frequently making the diagnosis difficult. Besides the usual allergic syndromes such as eczema, asthma or nasal symptoms, it may cause gastrointestinal symptoms, other skin manifestations, nervous system manifestations, etc. Of particular interest is the role of milk allergy in the aetiology of sudden death in infancy, infantile cortical hyperostosis, and in recurrent pulmonary infiltrations in infancy.

If the possibility of cows’ milk allergy is recognized it is frequently diagnosed. Diagnosis, for the most part is on clinical grounds, but if the physician considers other diseases in the differential diagnosis and evaluates them as carefully as he does the possibility of milk allergy, a correct diagnosis can usually be made. Once the diagnosis is made, treatment is relatively easy, consisting either in the withdrawal of milk from the diet or the use of milk in a modified form. Also, a good deal can be done in the field of prophylaxis – preventing the development of milk allergy in utero or in the newborn period, preventing it from becoming severe after it has developed and preventing it from going on to other forms of allergy in later life.

The prevention of some side-effects of cortico-steroid therapy

J. Landon, St. Mary’s Hospital, London, W. 2

The organic chemist, while succeeding in developing synthetic corticosteroids with minimum mineralo-corticoid activity, has been unable to separate therapeutic from many undesirable side-effects produced especially by high dosage levels.

Among the most serious complications of corticosteroid therapy are an increased incidence of dyspepsia and peptic ulceration, the impaired response to infection, adreno-

cortical atrophy and excessive protein catabolism resulting in such findings as a loss of muscle mass and osteoporosis.

Corticotrophin unlike corticosteroid therapy does not cause adrenal atrophy, and while having a higher incidence of pigmentation, acne and hirsutism, is associated with a lower incidence of gastrointestinal symptoms and excessive protein catabolism. Several of these differences may lie in the concomitant stimulation by corticotrophin of the adrenal androgens with their virilising and protein anabolic actions.

We and other workers have combined anabolic steroid with corticosteroid therapy in an attempt to ameliorate the protein catabolic effect of the latter. Several long-term metabolic studies have shown that methandienone, a powerful and relatively non-virilising protein anabolic steroid, prevented the negative nitrogen balance usually resulting from high dosage glucocorticoid therapy.

Our data is at present insufficient to assess the effect of methandienone on corticosteroid induced dyspepsia and peptic ulceration. In the three patients studied so far, methandienone has prevented adreno-cortical atrophy by prolonged high-dosage corticosteroid therapy, as evidenced by a normal response to corticotrophin. In a further patient, initially unresponsive to corticotrophin, methandienone appeared to cause a return of responsiveness.

Steroid therapy in chronic asthma

H. Morrow Brown, Derby Chest Clinic, 93, Green Lane, Derby

It was intended at the outset to deal with the diagnosis of chronic allergic asthma from chronic bronchitis and chronic bronchial asthma, with reference to the author's method of examination of the sputum for eosinophil cells. Emphasis was placed on the fact that unless the case is quite irreversible, allergic asthma does benefit from steroid therapy while chronic bronchitis and bronchial asthma do not.

A small demonstration of this method of sputum examination was set up.

In suitable cases, which were defined, the use of steroid therapy on a short term or a long term basis can be as safe as almost any other drug, provided that certain precautions are taken and that the methods of supervision and self-controlled dosage advocated by the author are followed. These methods were described in detail.

Total numbers of patients treated, incidence of complications and general comments on their progress were described. It was emphasised that anybody can prescribe steroids, but the greater problem is how to withdraw them and the importance of attempting to determine aetiological factors of the allergic state.

Finally, an account was given of a small trial of Betamethasone (Betnelan). Patients who were on a suitable dose of steroids or in whom the usual dose had become ineffective were changed over to this drug on a tablet for tablet basis. An account was given of the subjective reports, side-effects and the effects on ventilatory function.