Sent: 26 February 2007 09:00
To: Alana Miller

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Comments on "Corticosteroids for the treatment of chronic asthma in children under 12 years"

Previous personal experience with inhaled corticosteroids

I consider that my long-term involvement with ICS since 1970 entitles me to comment on this "Assessment Report", even though all my studies were 'open label' and therefore, by present day criteria, of no significance. Nevertheless, supported by similar studies from other investigators, a product licence was granted as soon as October 1972 by the Committee for Safety of Medicines, and by the FDA about two years later.

A clinical trial of **BDP** in Edinburgh from 1968 had shown no benefit, and by 1970 Allen & Hanbury were seriously considering discarding BDP as useless. I was asked to give the drug another chance, and commenced an open label trial in 1970 which included *only* patients who had eosinophils in their sputum, which means that their asthma is caused by allergy. I published the first successful clinical trials in adults in 1971 and in children in 1972, followed by several further studies in seasonal asthma, hay fever, and perennial rhinitis. My last report was in 1980 on treatment and outcomes of 145 children aged from 2 to 14 years who had been treated with BDP for from two to eight years.

Lack of consideration of allergic factors causing asthma in children

This assessment report concentrates entirely on therapy using various ICSs which suppress chronic allergic asthma but can never actually cure the condition. The almost total omission in the review of any mention of allergic factors as a significant and important cause of chronic asthma is a very serious deficiency . The importance of the identifying perennial environmental allergens, such as family pets and dust mites, and of avoidance measures in the home, are not even mentioned.

Environmental factors cannot be totally ignored because they are usually the very reason why ICS treatment has to be given. Patients are usually aware of the environmental possibilities today, even when their medical advisers may not be. Avoidance measures can decrease the incidence of severe attacks and also enable reduction of the dosage of ICS required for good asthma control, and thus less expenditure for medication .

Viral infections can trigger severe attacks of asthma in children, but allergy is the commonest cause of chronic asthma and perennial and seasonal rhinitis in children. The reason why ICSs are a more effective treatment for asthma in children than in adults is that more childhood asthma is caused by allergy, which is steroid sensitive. . Remodelling of the bronchi as a result of chronic childhood asthma will cause reduced reversibility and less effectiveness of ICS when they become adult asthmatics.

Lack of provision of allergy services in the NHS

However, this is no surprise when the general ignorance regarding allergic disease in the British medical profession is taken into account, and the lack of response of the NHS to the dramatic increase in incidence of all types of allergy in recent decades. In spite of a Parliamentary enquiry and yet another survey of the incidence of allergy the final response of the Ministry of Health has been to pass the responsibility for allergy to primary care, where the PCTs do not have the funds or the knowledge to set up any kind of allergy service. Guidelines correctly direct the most severe cases to a paediatric respiratory physician. Unfortunately , with few exceptions, the majority of paediatricians have no interest in allergic factors in the causation of asthma.

The nose and bronchi constitute a common airway

In recent years there has been gradual acceptance amongst respiratory physicians, mainly in Europe and USA that the nasal passages and the bronchi should be considered as one united airway. This review considers the bronchi only, and does not even mention perennial allergic rhinitis, which is very common in children, especially when asthma is also present. Perennial rhinitis, which is often overlooked in the UK, is frequently associated with allergic asthma, and is also treated with ICSs . Perennial rhinitis often has a severe effect on QOL and education, as illustrated by a series of photographs of the effects of chronic rhinitis on the facies of children in my website www.allergiesexplained.com Omission of any mention of upper airway dysfunction due to allergy, or its treatment with ICS, is regrettable.

The importance of new developments in aerosols

In recent years the substitution of HFA propellants for CFC has enabled the particle size of aerosols to be reduced to the extent that for the very first time it has become possible for ICS to access the whole bronchial tree. This really important development in therapy with ICS receives only passing mention in this review, in spite of the increasing number of publications presenting evidence that HFA aerosols of ICS reach the smaller airways.

On 1st February 2003 (vol 361 p 433) the Lancet published my letter to the editor on **"A neglected breakthrough in asthma therapy."** and I quote and italicise portions which seem relevant :-.

"Results of studies of radiolabelled BDP suspended in CFCs have shown that only 13% of inhaled BDP is retained in the lung, mostly in the larger bronchi. With BDP dissolved in HFA an ultrafine aerosol is produced of which 53% is *deposited evenly throughout the lungs, thus reaching the peripheral airways. The importance of this finding is that the smaller bronchi can be accessed and treated with inhaled corticosteroids.*

The peripheral airways have been shown to be a major site of inflammation and obstruction in asthma, therefore *treating the whole bronchial tree should prevent some patients with reversible asthma from slowly developing irreversible chronic obstructive pulmonary disorder over many years.* ***Furthermore, these ultrafine aerosols ought to improve long-term outlook of children with chronic asthma who need indefinite steroid aerosols."***

The change to HFA propellants, which may have been brought about by the effects of CFCs on the ozone layer rather than the improved characteristics of the aerosols, does not appear to have been recognised as the first real advance in steroid aerosol therapy for asthma in many years, especially when treating children. This new ability to suppress an allergic reaction in the *whole bronchial tree* must be really important to the prognosis of children with serious chronic asthma who are likely to be dependent on ICS for life, because remodelling and progressive deterioration may be prevented, but long-term observations on large groups will be necessary to prove this hypothesis.

Why is this investigation necessary? What is its purpose? What outcome is expected?

I have carefully perused this report without finding any valid reason why, after over thirty years of general use in treating childhood asthma, it is necessary to review an established method of treatment which has an extremely low incidence of side-effects. The mandatory change from CFC to HFA propellants has resulted in aerosols producing ultra-fine particles of steroid which suppress allergic reactions throughout the whole bronchial tree for the first time. **This major development in aerosol therapy renders this report out of date already**.

The preparation of this report, which involved at least thirty highly qualified people, must have cost a great deal of money and an enormous amount of time, both of which could have been better spent elsewhere. How many of those people are involved in actually seeing and treating children with asthma, and why do there appear to be no paediatricians amongst those involved in the preparing the report?

The almost total absence of mention of the causes of allergic asthma, and the emphasis on suppressive therapy in this review is symptomatic of the prevailing ignorance of the majority of the British medical profession of the increasing importance of allergy as a cause of illness and poor quality of life in our children, many of whom will grow up to be chronic asthmatic adults.

The meeting on the 28th April last, which I attended as a representative of the Charity Action Against Allergy, seemed to me to be a similar waste of time and money, especially as no microphones were available. This deficiency made it very difficult to hear statements being made at the far end of a very large room, especially when the representatives were female.

I am very pleased to know that, according to your letter of 17th January, my comments will be sent to all consultees and commentators as part of the evaluation report, will be tabled at the Appraisal Committee meeting, and will be published on the NICE website approximately 20 days after the first Appraisal committee Meeting

Yours very sincerely,
