'ACTIFED'—A CLINICAL IMPRESSION

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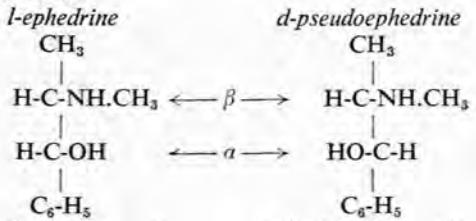
Some years ago I described a series of cases under the title 'Asthma in young boys' in this *Journal*.[1] I then showed that a combination of drugs, such as pseudoephedrine and an antihistaminic, should have most beneficial effects if given to asthma sufferers every night before going to sleep, provided it was done over long periods. Messrs. Burroughs Wellcome and Co. Ltd., taking cognizance of my article, informed me that they, too, had investigated the effect of such a combination of drugs in patients in whom the upper respiratory tract was involved idiopathically, or through allergy or infection.

The commercial name given to this combination of drugs is 'actifed'. It contains 30 mg. of pseudoephedrine, and 1·25 mg. of triprolidine hydrochloride which is a powerful antihistaminic. The pseudoephedrine combination is interesting; I find it is less toxic and has fewer side-effects than ephedrine hydrochloride. Also it has shown less central stimulation and vasopressor effect. I particularly wish to give full details of this drug as found in the literature, because I feel that it has not been sufficiently investigated and could be of great benefit where a substitute for ephedrine hydrochloride is sought, especially in view of the fact that it is less toxic and has less side-effects.

D-PSEUDOEPHEDRINE

Ephedrine contains two asymmetric carbon atoms and therefore has 6 synthetic isomers, viz. *l*, *d* and *dl* ephedrine, and *l*, *d* and *dl* pseudoephedrine.

Two of these also occur naturally—*l*-ephedrine and *d*-pseudoephedrine—and the chemical difference between them lies in the relation between the hydroxyl group on the α- and the methylamino group on the β-carbon atom of the side chain, the groups being close to each other in ephedrine and removed from each other in pseudoephedrine, as shown here:



d-Pseudoephedrine, the natural alkaloid, is used in actifed because it is almost as potent, weight for weight, as ephedrine, but produces neither the same degree of central stimulation nor the vasopressor effect. The 1949 *British Pharmaceutical Codex* states: '*d*-Pseudoephedrine resembles ephedrine qualitatively, but its effects, particularly on the blood pressure, bronchi and higher centres, are weaker. It is less toxic and has fewer side effects'.

Action

d-Pseudoephedrine is an orally effective nasal decongestant which takes effect 15 - 30 minutes after oral administration. The mucous membrane of the entire respiratory tract is gently, but promptly, decongested through action on sympathetic nerves and smooth muscle. With its simultaneous bronchodilating action, *d*-pseudoephedrine facilitates free breathing by opening the airway from nostrils to alveoli. The systemic route of administration obviates the use of topical preparations, thereby protecting the delicate inflamed nasal mucosa from additional trauma. Furthermore, it gives desirable prophylaxis against middle-ear complications by reaching and decongesting the Eustachian tubes.

Nasal Decongestion

d-Pseudoephedrine restores patency of the nasal passages by shrinking the engorged nasal mucosa and quickly eliminating tissue hyperaemia and oedema. 'Its dilator action on the bronchioles, as well as its contracting action on the mucous membrane of the nose, do not essentially differ in potency from that of ephedrine'.[2]

Bronchodilation

In clinical use,[2,3] and in laboratory studies,[4] the bronchodilator action of pseudoephedrine appears to be quite marked. Complementing the bronchodilating action, pseudoephedrine decongests the mucosa of the tracheobronchial tree.[2,3]

Toxicity

In animal studies pseudoephedrine has been found to be nearly 50% less toxic than ephedrine. The LD_{50} for mice is 700 mg. per kg.

CASE REPORTS

Of 30 patients for whom I prescribed actifed, the majority responded favourably and could go about their duties undisturbed. These patients suffered from allergic rhinitis, bronchial catarrh, asthma, sinusitis, postnasal drip, hayfever and Eustachian-tube blockage. Also, there were patients with chronic disease of the upper respiratory tract, where symptoms had persisted despite operation or bombardment with antibiotics. My trial has now continued for a period of just over a year, and I propose to describe in brief some patients for whom I have prescribed actifed.

Case 1

European male, aged 70 years: He had a history of sinus infection for 10 years, and was treated with antibiotics and sinus puncture with incomplete relief. His condition gradually developed into a persistent bronchitis and bronchial catarrh as well as ?septic arthritis. Sensitivity tests were done against organisms from his sputum, and so many antibiotics were used in an attempt to clear his upper respiratory tract that he developed moniliasis. The sinusitis and bronchitis persisted and eventually cortisone was tried as well. He was given actifed, 1 tablet twice daily, and thereafter was found to be completely relieved of bronchial catarrh and wheezing chest as well as postnasal drip. He still expectorates a small amount of sputum in the morning. At present he finds

that 1 tablet on alternate mornings is enough to control his symptoms.

Case 2

European male, aged 49 years: He came from the Congo to live in Sea Point, but experienced severe chest wheezing at night, a painful dry cough and nasal blockage. During the day he was quite normal. He had never had any illness like this before, except bronchitis 2 years previously. On examination he had typical bronchospasm. At first it was necessary to give him an injection of adrenaline, but I decided to give him actifed tablets, 1 twice daily for 2 days and thereafter 3 times a day. With the exception of slight drowsiness his symptoms were completely relieved.

Case 3

European male, aged 40 years: He complained of deafness of his left ear, which had wax in it, but despite syringing there was no improvement. In addition he had an old-standing suppurative otitis media of his right ear. I referred him to an ear, nose and throat specialist who diagnosed a blocked left Eustachian tube. He politserized him without improvement. I decided to try actifed, and within 5 days his Eustachian-tube deafness had completely cleared up. In the patient's own words 'it simply was wonderful!'

Case 4

European male, aged 36 years: He consulted me in 1956 with a diagnosis of catarrh of the upper respiratory tract. Sensitivity tests showed him to be sensitive to house dust and the pollen of flowers. At this time he was using an adrenaline spray as well as antihistaminics, but this treatment made him very tired and depressed. He had moved from where he lived previously to Sea Point. In addition he had developed a bronchospasm at night. Further treatment with antibiotics, an electric air filter and warmer in his room, plus sprays and antihistamine did not relieve him. I suggested that he should try actifed, and for the past 6 months he has continued to use it. It has helped him more than any other treatment he has had up to date. He stated that he could now sleep undisturbed at night and that his bronchospasm and nasal blockage are definitely relieved.

Case 5

European girl, aged 8 years: She had had nasal disturbances since she was 5 years old. She had a tonsillectomy, but this did not improve matters. Sensitivity tests with antibiotics, inhalations and breathing exercises were also tried, but they brought little relief to the nasal disturbances. An X-ray revealed definite maxillary-sinus involvement. It was necessary to have a sinus operation performed, despite her age. There was some improvement, although the child was troubled at school because her teacher continually reprimanded her for blowing her nose. I prescribed actifed for her and found that her nasal disturbances were gradually controlled by its use. Also, it helped to tide her over until she could have a further operation to her sinuses, which have since cleared up.

Case 6

European female, aged 20 years: She suffered from bronchospasm at night. Her symptoms were nose blockage, slight cough, and a general tightness of her chest. Despite the use of 'amesec' capsules, adrenaline injections and desensitization with azoprotein, I was obliged eventually to prescribe cortisone to relieve her symptoms for 6 weeks. When the course of cortisone was completed, her symptoms gradually came back. I found that in prescribing actifed, in addition to a much smaller dose of cortisone than formerly, I managed to control her symptoms for the last 6 months.

Case 7

European male, aged 70 years (seen by Dr. J. Sonnenberg): He states that for the past 6 months his nose just ran without warning. He also developed bronchospasm. His nose was cauterized, but this gave only temporary relief. On examination he appeared to have typical allergic rhinitis. He was given actifed, 1 tablet twice daily, with almost dramatic improvement.

CONCLUSION

The 7 patients I have mentioned represent a fair cross-section of my trial cases helped by actifed treatment. It is not a cure, except in seasonal cases, but it is certainly a very good preparation in the symptomatic treatment of upper respiratory conditions, especially when a patient has been through a long period of illness with many different forms of treatment and the doctor is rather at a loss for something new. I have noticed no side-effects, except slight drowsiness at the beginning of treatment. This passes off after a few days' treatment.

I must point out that actifed is not a blunderbuss combination, containing only pseudoephedrine and triprolidine. If an antipyretic is necessary, aspirin compound could be given in addition.

Since this article was prepared, Burroughs Wellcome have brought out actifed tablets in half the strength used in this trial. This will do away with the drowsiness and allow for greater flexibility in dosage.

I wish to thank Prof. F. Forman, Prof. N. Sapeika, and Dr. I. Grayce for kindly reading this paper and for their useful comments. I also wish to thank Burroughs Wellcome and Co. (S.A.) Ltd. for supplying the tablets used.

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