Practolol and deafness

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Stimulation of the sympathetic nerves to the heart increases the cardiac rate and augments myocardial contractility. The beta-adrenoceptor blocking agents specifically block these effects and they are widely used in the control of cardiac dysrhythmias and angina pectoris, effectively reducing the frequency and severity of anginal symptoms.

One of these is Practolol, manufactured by Imperial Chemical Industries (I.C.I.) Limited and prescribed under the proprietary name of 'Eraldin'. A licence for this drug was issued by the Department of Health only after extensive clinical trials, the results of which were reviewed by the Committee on Safety of Drugs; and it had been prescribed for, and safely used by, hundreds of thousands of patients, both in the United Kingdom and overseas, before some totally unexpected side-effects were found to follow its long-term use. These included skin rashes, often psoriasiform; ocular symptoms, amongst them kerato-conjunctivitis (and very rarely blindness); 'plastic' peritonitis; recurrent ulceration in the mouth and nose; and *deafness*.

One of the Adverse Reaction Series (No. 11, 1975) of the Committee on Safety of Medicines reported 25 complaints of deafness from practolol by the end of 1974.

Wright (1975) reported that 15 out of 27 patients with ocular disease secondary to practolol had tinnitus and/or deafness and that these symptoms came on several months after lesions of the eye and skin. Simple tests suggested mixed deafness, five patients needed treatment for serous otitis media, and two became profoundly deaf. In a later paper, Wright and Fraunfelder (1976) mentioned the occasional complication of fibrinous peritonitis.

Inman (1977), in a recent letter to one of the present authors, has stated that the actual number of patients reported to have deafness up to 22 June 1977 was 94, out of a total of approximately 1400 for whom adverse reactions have been reported to the Committee on Safety of Medicines. Of these 94 cases, deafness was the main complaint in only 13, the remaining 81 having deafness in addition to more serious side-effects.

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Many doctors, including otologists, are still unaware of these adverse effects of practolol, and unfamiliar with their exact nature. We are prompted, therefore, to record our combined experience of ten cases of deafness following the use of this drug. Three of these are cases of mixed deafness, six entirely sensori-neural, and one of them dubious.

Mixed deafness following the use of practolol

As previously reported by Wright (1975) and by Wright and Fraunfelder (1976), several cases of deafness following the use of practolol have exhibited a mixed sensori-neural and conductive hearing loss, the latter being due commonly to the presence of serous fluid in the middle ear.

Two of our three cases of mixed deafness had proven serous otitis media, one in both ears, the other in one only.

Case 1

Mr. R.G.G., aged 65 years, was examined on 12 February 1976 (R.F.McN.J.).

He suffered a coronary thrombosis in September 1970, and treatment with practolol was begun in 1971.

No side-effects were noticed until the summer of 1972, when he began to have inflammation in his left eye and later in the right eye. In September of the same year, he suffered from bronchitis with pleurisy and shortly afterwards he developed, first a left-sided and later a bilateral facial palsy; in October he was treated as an in-patient for a psoriasiform skin rash. He also had occasional but violent attacks of abdominal pain, relieved by vomiting.

Impairment of hearing was first noticed in April 1973, but the drug was not withdrawn until June 1974.

When examined on 12 February 1976, his hearing was severely impaired and occasionally he had a rapidly repeating bell-like tone in his ears; although he could not whistle, his facial movements were otherwise more or less symmetrical and satisfactory.

Both tympanic membranes were slightly retracted and had a marked yellow sheen. Tests of hearing showed a severe bilateral mixed deafness (Fig. 1A) and myringotomies were recommended.

These were performed, at his local hospital, in April 1976, when serous fluid was removed by suction and grommets were inserted. There was a marked improvement in his hearing for 10 days, but the deafness then returned in his right ear and a further grommet was inserted on that side on 16 December 1976. When seen later in the same month, the left grommet was patent but the right was again blocked and there was evidence of residual fluid in the right middle ear.

A further audiogram at this time (Fig. 1B) showed a sensorineural hearing loss only in the left ear, with a mixed deafness in the right.

So far as we are aware, the facial palsy in this case was unique and the fact that it was bilateral would seem to make it possible that this was yet another side-effect of the practolol, rather than a coincidental Bell's palsy; but this is by no means certain and the question must remain an open one.

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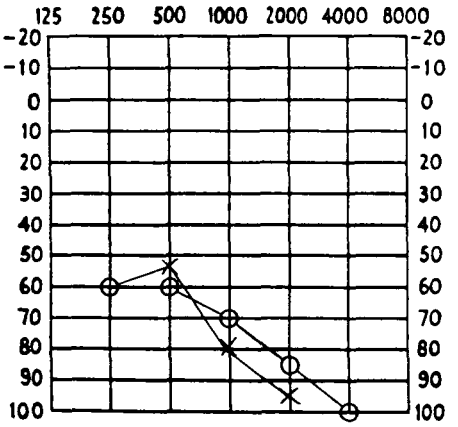


FIG. 1a.

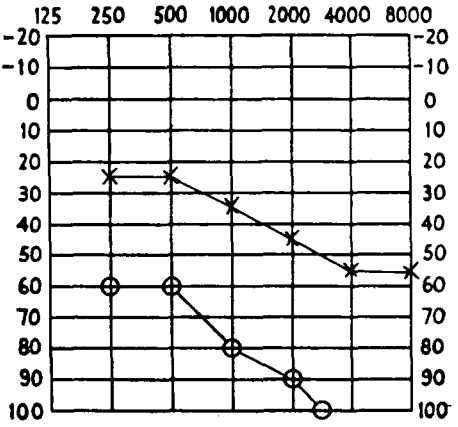


FIG. 1b.

The abdominal pains from which this patient suffered may well have been caused by a 'plastic peritonitis', another reported complication; and the case demonstrates many of the drug's other well-documented side-effects; a psoriasiform skin rash, kerato-conjunctivitis, pleurisy, and mixed sensorineural and conductive deafness, the latter due to serous otitis media.

Case 2

Mrs. M.E.A., aged 68 years, was seen on 8 November 1976 (J.C.B.).

She was admitted to Northwick Park Hospital in 1971 with anginal symptoms, and treatment with practolol was begun immediately.

She received the drug four times a day, and eighteen months later she experienced a feeling of 'sand' behind both eyes. Vision was also affected and she developed a skin rash.

Three years after starting treatment with practolol, the patient became gradually aware of some difficulty in hearing, more in her right ear than in the left. No further change in her hearing was noticed after the drug was stopped a year later.

When examined on 8 November 1976, the tympanic membranes were intact, but there was a yellowish discolouration in the right side which suggested that there was fluid in the middle ear. With a 512 Hz tuning fork the Rinne test was positive in the left ear, negative in the right, and the Weber response was referred to the right ear. An audiogram (Fig. 2A) showed a moderate sensorineural hearing loss in the left ear, with a mixed sensorineural and conductive deafness in the right.

A right myringotomy was performed at the Royal Free Hospital on 20 February 1977, when a large quantity of serous fluid was removed from the middle ear by suction and a grommet was inserted.

There was immediate marked improvement in the hearing in her right ear (Fig. 2, B) which has been maintained to the present time.

Again the presence of ocular symptoms and skin rash preceded the subjective onset of deafness, sensori-neural in one ear and mixed in the other, by many months.

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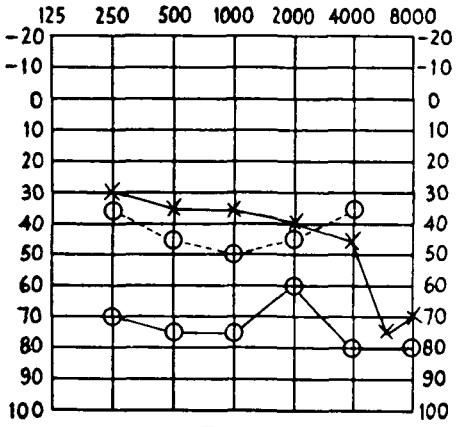


FIG. 2a.

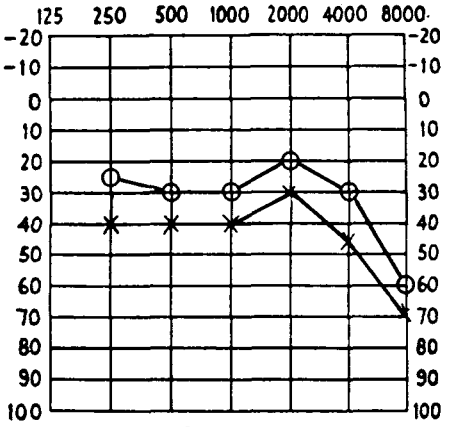


FIG. 2b.

Case 3

Mr. H.C.D., aged 63, a retired aircraft engineer, was seen on 18 April 1977 (V.T.H.).

He received practolol three times a day for 3 years.

Three months after starting the drug, a skin rash developed on the back of his neck, and one month later he noticed an intolerance to bright light. Two years after starting treatment he began to suffer from constipation and intermittent upper abdominal pains.

At about the same time he began to notice a gradual deterioration of hearing, with a feeling of blockage in the left ear.

The skin rash cleared two weeks after the drug was stopped, but the intolerance to bright light continued.

When examined on 18 April 1977, both tympanic membranes looked healthy and the Eustachian tubes were both patent. With tuning forks of 256 and 512 Hz the Rinne test was positive in the right ear, neutral in the left; and the Weber response was referred to the left ear. Although there was no visual evidence of fluid in the left middle ear, an audiogram (Fig. 3) showed a slight sensori-neural hearing loss in the right ear, with a mixed deafness in the left.

Although this patient had worked as an aircraft engineer, there was no evidence in the audiogram that noise had been a significant factor in the production of his deafness; and the fact that he had suffered from no hearing loss before he received the drug and that his deafness was preceded for many months by a skin rash and ocular symptoms make it likely that his hearing loss was caused, at least in the left ear, by the practolol.

Sensori-Neural Deafness following the Use of Practolol

Six of our cases suffered from varying degrees of sensori-neural hearing loss after treatment with practolol.

Case 4

Mr. L.E.B., aged 56, was seen on 19 May 1976 (V.T.H.).

He received practolol from January 1971 to August 1974.

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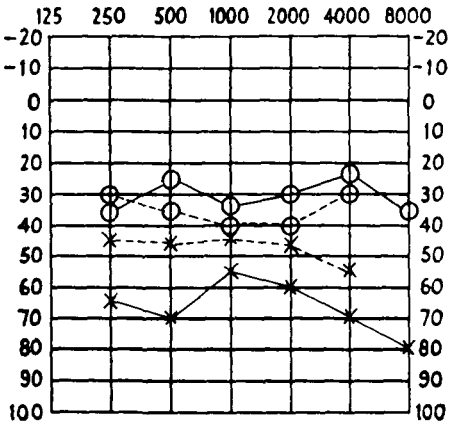


FIG. 3.

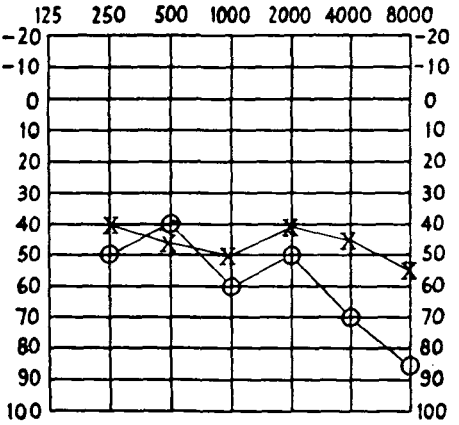


FIG. 4.

Late in 1973 he developed 'rectal trouble', and in January 1974 he had dryness of the skin, especially on the scalp, hands and feet.

At about the same time he developed an intermittent left-sided tinnitus—'like a fog horn', which lasted for 15-20 minutes at a time. This symptom improved when the drug was stopped, but it still continues. He noticed some deterioration of hearing over the same period.

On examination, the ears appeared healthy, but an audiogram (Fig. 4) showed a moderately severe sensori-neural hearing loss in both ears, affecting the right ear more than the left.

Case 5

Mr. R.G., aged 56, was seen and examined on 17 January 1977 (V.T.H.).

This patient received practolol for eight months in 1973.

Whilst taking the drug he developed a generalized rash and soreness in the eyes. He also had four episodes of swelling in the right pinna, each one lasting for one week.

He developed intermittent deafness and a sensation of blockage in both ears during his treatment, and these symptoms have persisted.

On examination, the ears looked healthy, but an audiogram (Fig. 5) showed high-frequency sensori-neural hearing losses in both ears, affecting the left more than the right.

Although the shape of his audiograms was somewhat suggestive of noise-induced hearing loss, he had never worked in a noisy environment.

Case 6

Mrs. O.P., aged 80, was seen and examined on 11 February 1977 (V.T.H.).

She received practolol twice a day from 1970 to 1975.

She developed a dry mouth and throat, with recurrent mouth ulcers, 3 months after starting the drug, and in 1972 her eyes became dry and she developed a rash on her face.

In 1975 she began to suffer from left-sided tinnitus and deafness.

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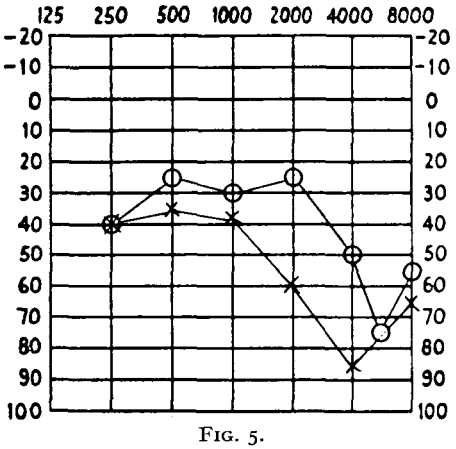


FIG. 5.

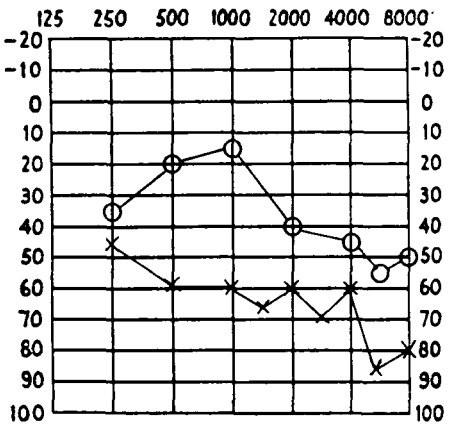


FIG. 6.

On examination both ears were healthy, but an audiogram (Fig. 6) showed a bilateral high-frequency sensori-neural deafness, affecting the left ear much more than the right.

Although the hearing loss in her right ear was probably due to simple presbyacusis, it is likely that the difference in hearing between the two ears was due to a toxic effect of practolol on her left ear.

Case 7

Mrs. K.B., aged 76, was seen on 22 March 1976 (V.T.H.).

She was treated with practolol from 1971 to 1974.

After a few months on the drug, her vision began to deteriorate, and a diagnosis of kerato-conjunctivitis was made.

An operation had been performed on her right ear twenty years earlier and she had been very deaf in that ear since the surgery. She began to develop a progressive deafness in her left ear in 1975.

On examination there was a healthy radical mastoid cavity in the right ear, but the left was normal. An audiogram (Fig. 7) showed a mixed deafness in the right ear, with a moderately severe sensori-neural loss in the left.

Although some at least of the hearing loss in her left ear may have been due to simple presbyacusis, the opinion was expressed that practolol probably contributed to it.

Case 8

Mr. C.J.W., aged 53, was first seen on 17 December 1976 (D.W.).

He was treated with practolol from July 1969 to February 1975.

In 1972 he had soreness, dryness and grittiness in the eyes, with uncontrollable watering; and his vision was blurred at times. There was a rash on his right thigh and itchiness of the skin over his shoulder blades. He also had, and still has, dryness and cracking of his tongue, and occasional abdominal pains with stomach cramps and constipation.

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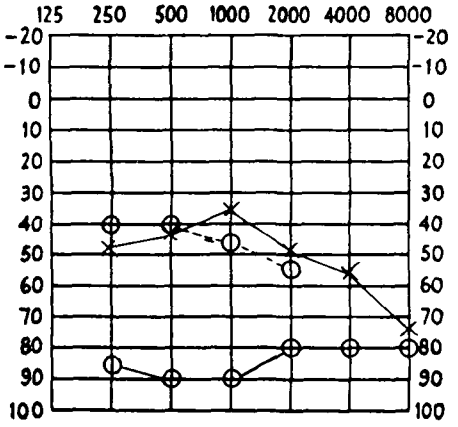


FIG. 7.

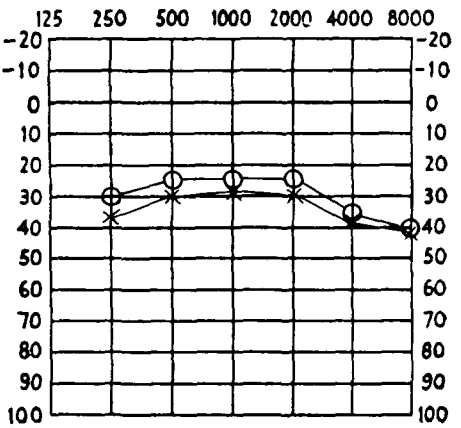


FIG. 8.

Early in 1972 he experienced a high-pitched whistling sound in both ears, affecting the left more than the right. Although he was able to manage well with normal conversation, he had some difficulty in hearing people when they spoke behind him.

On examination, on 24 February 1977, both tympanic membranes were normal and there was no clinical evidence of serous otitis media. The Rinne test was positive in both ears with a tuning fork, and an audiogram (Fig. 8) showed a bilateral sensori-neural hearing loss averaging 25-30 dB in the speech frequencies. Stapedius reflexes were elicited at a slightly lower level than one would expect with such a degree of deafness, thus indicating possible recruitment.

Case 9

Mrs. A.E., aged 71, was seen on 12 July 1977 (D.W.).

She was treated with practolol from 1972 to 1975.

At about the time that the drug was discontinued, or within three months of this time, her vision became hazy, with almost complete loss of vision at times, and there was irritation in both eyes. She also had irritation of the skin of her right knee and right shoulder, of her back and of the hypothenar eminences of both hands; and for the last two years she has had almost continual attacks of abdominal pains.

Soon after the practolol was withdrawn, this patient noticed that her hearing was muffled and she developed a high-pitched tinnitus in both ears. She had difficulty in conversing with more than one person.

When she was examined, on 12 July 1977, the tympanic membranes were intact, there was no clinical evidence of secretary otitis media and the Rinne test was positive in both ears with a tuning fork. An audiogram (Fig. 9, A) showed a moderately severe hearing loss in both ears.

This case is of further interest because an audiogram (Fig. 9, B) had been done on 27 June 1970, before the patient received any practolol. At that time, there was evidence only of early presbyacusis.

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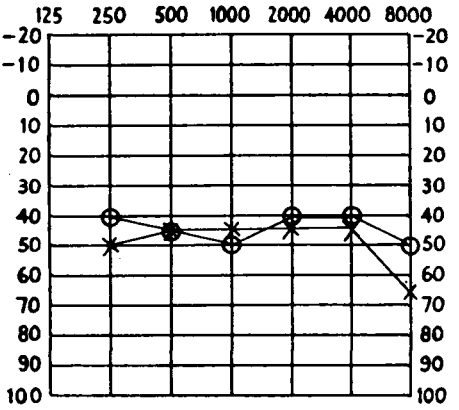


FIG. 9a.

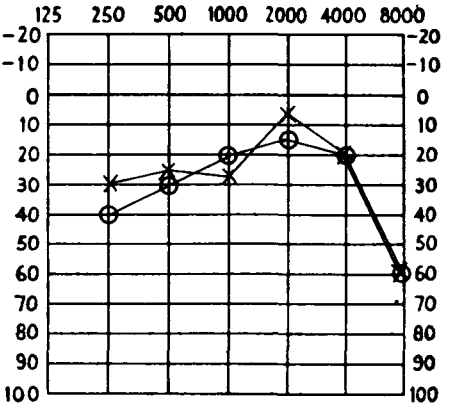


FIG. 9b.

One dubious case of deafness following the use of practolol

Case 1

Mr. H.O'M, aged 61, was seen and examined on 22 April 1977 (J.C.B.).

He was treated with practolol from June 1973 to April 1975 for tachycardia following a 'heart attack'.

In the summer of 1974, he began to have burning and soreness of his eyes, especially in the right eye; there was also some soreness in the left ear and flaking of the skin over the left ankle.

At about the same time, he noticed that he was having to ask people to repeat things as he was not hearing well, especially in his left ear.

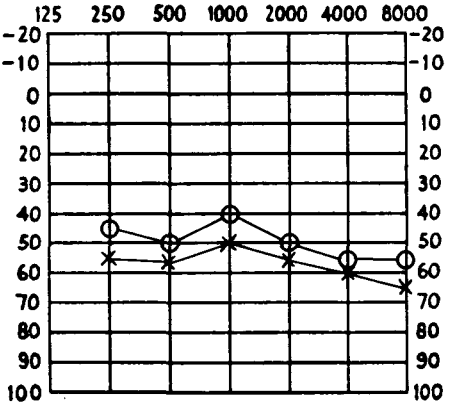


FIG. 10.

On examination both tympanic membranes were healthy, the Rinne test was positive in both ears with a tuning fork, and an audiogram (Fig. 10) showed a moderately severe degree of sensori-neural hearing loss in both ears, affecting the left slightly more than the right.

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Practolol and deafness

Superficially the combination of ocular symptoms, skin rash and hearing loss following the use of practolol would suggest that all these symptoms were probably caused by the drug, but there were certain factors which made it difficult to form a firm opinion about the cause of deafness in the present instance; and each or all of these may complicate the issue in all such cases.

In the first place, this patient had spent one period of his life in the 1930s as a sheet metal worker, and noise-induced hearing loss may have to be considered. In the present case, however, there was no subjective difficulty in hearing until forty years later and the shape of the audiogram was unlike that seen after noise exposure.

More difficult to assess was the possible part played by ageing in Mr. O'M's deafness for, at the time of its onset, he would have been 57 or 58. But his hearing loss is considerably greater than one would expect at that age, and he was the youngest of siblings, none of whom has or had any difficulty in hearing. Hence it is unlikely that age played any significant part in his quite severe deafness.

Characteristically, in several of the few cases so far reported, the deafness due to practolol has become manifest only some time after the onset of symptoms and signs in skin and eyes; yet in the present case all these symptoms developed simultaneously.

This is not to deny that all of them may well have been caused by the drug, but this somewhat dubious case does serve to emphasize the fact that, in the absence of routine hearing tests *before* the use of any new drug, a cause-and-effect relationship may be difficult to establish.

Discussion

Practolol ('Eraldin') is one of many beta-adrenoceptor blocking agents which have been used for the symptomatic control of anginal symptoms, others including propranolol ('Inderal') and oxprenolol ('Trasicor'); but practolol has now been withdrawn except in the injectable form which is available in Coronary Care Units for the urgent treatment of life-threatening arrythmias in the immediate post-infarction stage.

The Committee on Safety of Medicines has received many reports of adverse reactions to beta-blockers other than practolol, and by the end of 1976 these had included 133 skin rashes, about one-half of which resembled psoriasis, and 74 ocular symptoms and signs, the majority of which have been mild cases of conjunctivitis or dryness of the eye.

Practolol, however, seems so far to be unique in its ability to cause deafness. In a significant proportion of these cases, this symptom is caused by a mixture of sensori-neural hearing loss with conductive deafness, sometimes due to serous otitis media, in one or both ears. The cause of this latter condition remains obscure, but it should be said that the nose and nasopharynx were healthy in all the cases reported in the present paper.

Characteristically the deafness has been noticed only many months, and sometimes years, after the appearance of other side-effects, notably

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in the skin and eyes; and other adverse reactions include bronchitis and pleurisy, fibrous or 'plastic' peritonitis, and recurrent ulceration in the mouth and nose. One of our cases (Case 1) was unique, so far as we know, in suffering from bilateral facial palsies which recovered satisfactorily after the drug was withdrawn.

One must be mindful of other factors before attributing a hearing loss to the effects of practolol; in particular, one must enquire about the use of other ototoxic drugs and previous noise exposure. Age, too, may be an important consideration, for many of the patients receiving the beta-blocking agents belong to older age groups; in the present series of 10 cases, for example, the patients' ages ranged from 53 to 80 years, with a mean age of 65.

Finally, it must be emphasized that deafness, in common with all or most of the other adverse effects of practolol, usually develops only after many months or several years of treatment with this drug.

Summary

Practolol ('Eraldin') is a beta-blocking agent whose prolonged use may result in the appearance of untoward side-effects, notably ocular symptoms, skin rashes and deafness.

We report ten cases of deafness due, or thought to be due, to practolol; and in all except three of these cases (8, 9 and 10), the deafness became manifest many months after the appearance of lesions in the skin and eyes.

Progression of any hearing loss caused by this drug seems to be arrested by its withdrawal.

Otologists are urged to report any suspicious cases to the Committee on Safety of Medicines, Finsbury Square House, 33/37A Finsbury Square, London EC2A 1PP.

Acknowledgements

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