Deafness in Acromegaly*

By Stephen Richards (Cardiff)

Acromegaly is caused by the excessive secretion of growth hormone by the alpha cells of the anterior pituitary. During the last 10 years the study of the disease has been placed on a much sounder scientific basis by the isolation of human growth hormone in its pure form by Raben and his associates (1962). This led to the development of an accurate method of measuring the concentration of human growth hormone in the plasma by radio-immune assay by Glick *et al.* (1963) in the United States and by Hunter and Greenwood (1964) in this country.

Various authors (Escat, 1922; Nager, 1933 and Cawthorne, 1947) have suggested that the endocrines play an important part in the development of otosclerosis. If circulating hormones are to be implicated in the activation of potential otosclerotic foci, growth hormone, which stimulates the growth in numerous tissues including bones, would appear of greatest possible significance.

Only one recorded case of deafness in a patient suffering from acromegaly has been found in the literature of the past 10 years. This was reported by Otto Menzel in 1966. A 72-year-old male patient, suffering from acromegaly, was found to have a sensori-neural hearing loss which amounted to some 30–40 db. in the lower frequencies with a further deterioration in the higher tones. Speech discrimination was poor in both ears. Menzel was of the opinion that the deafness was caused by pressure on the acoustic nerve by bone hypertrophy and narrowing of the internal auditory canals.

It is obviously of considerable interest to ascertain whether there is an increased incidence of otosclerosis in acromegaly, and the investigation now reported was carried out to investigate the hearing levels in 15 patients suffering from this disease.

Method

15 patients referred to the Surgical Unit of the United Cardiff Hospitals for the investigation and treatment of acromegaly, were studied. All had well-marked and sometimes gross clinical features of the disease. Full clinical documentation had been carried out and all patients had been investigated thoroughly biochemically, including the estimation of

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plasma growth hormone levels by radio-immune assay. This estimation was carried out by Dr. Fred Greenwood in the Imperial Cancer Research Laboratories.

Each patient was seen by an Otologist and a thorough otological examination made after taking a careful history. They were then further investigated by means of pure-tone audiometry and Hallpike caloric tests.

Results

The series of acromegalic patients studied is detailed in Fig. 1 from which it is noted that:

1. Nine patients were female and 6 male.
2. Their ages varied from 31 to 64 years.
3. The duration of the disease varied from $3\frac{1}{2}$ to 36 years.
4. The blood pressure, expressed as the average of the systolic and diastolic readings, was moderately raised in most patients.

Patient No.	Age	Sex	Duration of Acromegaly (Years)	Average Hearing Loss (db.)	Diabetes	Average Blood Pressure (mm.)	Plasma Growth Hormone (ng. per ml.)
1	31	F	$3\frac{1}{2}$	10	—	180	Not yet available
2	33	M	11	18	—	142	128
3	36	F	18	17	D (Mild)	110	65
4	45	M	17	24	—	135	52
5	51	F	6	21	—	150	46
6	51	F	9	32	D	100	335
7	51	M	16	55	—	115	84
8	53	M	17	26	—	105	2
9	55	F	6	32	—	150	14·2
10	57	M	4	25	—	100	24·5
11	58	F	16	21	—	150	29
12	59	F	28	41	D	115	1,145
13	61	F	8	100	—	160	59
14	63	F	16	16	—	113	65
15	64	M	36	70	D (Mild)	115	13

FIG. 1.

Shows the details of age, sex, duration of acromegaly, average hearing loss, whether diabetes present, average blood pressure, and plasma growth hormone level in the 15 acromegalic patients studied.

5. Four patients were diabetic. Two were mild and did not require any insulin therapy, two were severe and of long standing.

6. The fasting growth hormone levels showed wide variation ranging from 2 to 1,145 nannograms. The normal level from Dr. Greenwood's laboratory of fasting growth hormone is from 0 to 10 and two of the patients (Nos. 8 and 15) had levels in this range. Both these patients had had irradiation of the pituitary.

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Details of the growth hormone results in these patients have been previously reported (Greenwood *et al.*, 1965).

7. The caloric test which has not been recorded in this Figure was normal in all patients.

8. The hearing levels shown are the average for pure-tone thresholds by air conduction in the two ears at 0·5, 1, 2 and 4 kilocycles.

All the patients had normal tympanic membranes except No. 7 who had a chronic suppurative otitis media in one ear. Both ears of patients 13 and 15 and one ear of patient 4 showed marked conduction deafness with normal tympanic membranes. In five ears, therefore, there were strong reasons for diagnosing otosclerosis affecting the stapedial footplate. Two patients (Nos. 13 and 15) have had an exploratory tympanotomy operation carried out in one ear and, in each instance, the footplate of the stapes was found to be fixed by advanced Grade III otosclerosis. The appearance of the bone at operation in each case was indistinguishable from what we see in classical otosclerosis of the stapes. In both these ears, the footplate was removed, replaced by a prosthesis and the bone fragments sent to the pathology department for microscopy. Figs. 2 and 3 show the microscopic appearances of the removed footplates. The

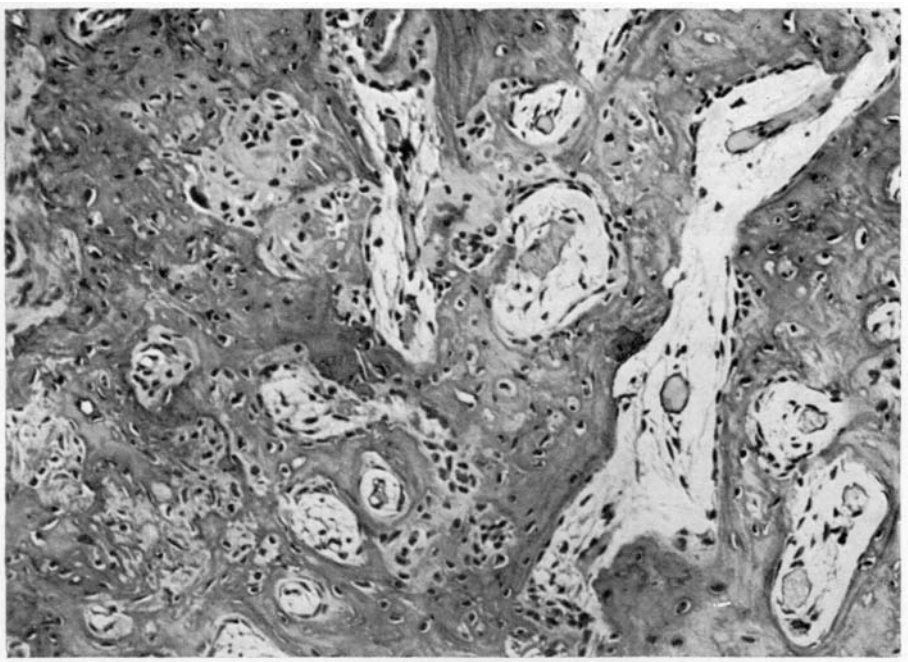


FIG. 2.

Shows the structural changes in the stapedial footplate removed at operation in patient No. 13. The photograph shows evidence of active otosclerosis with a high degree of vascularity and cellular activity. This patient had a high level of circulating plasma growth hormone (59 ng/ml.).

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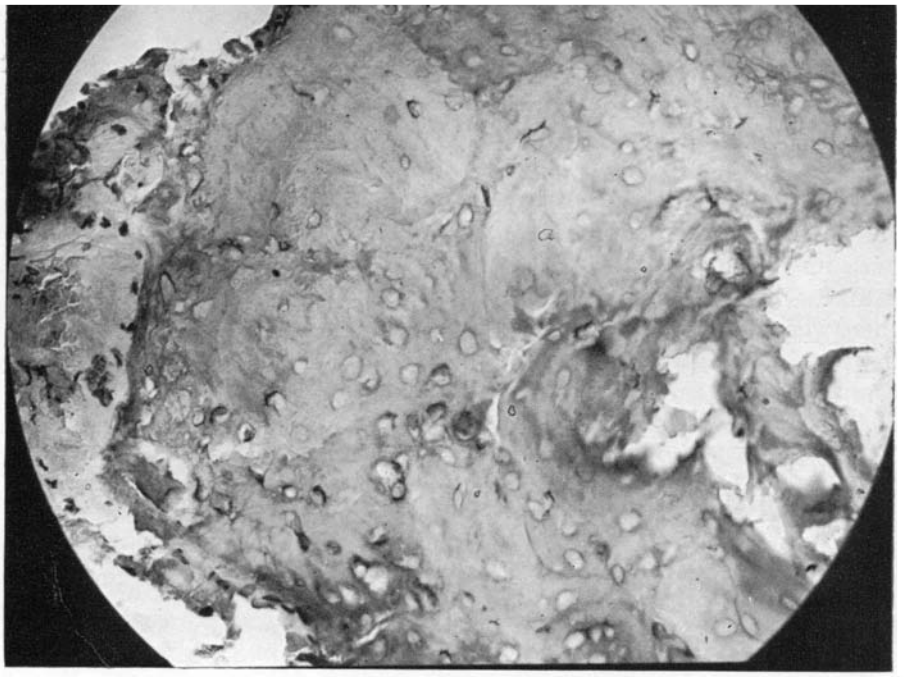


FIG. 3.

Shows the microscopic changes in the stapedial footplate removed at operation in patient No. 15. It shows dense otosclerotic bone with poor vascularity and a low level of cellular activity. This patient had a low level of circulating growth hormone (13 ng./ml.).

first one shows very active otosclerosis and the second one shows inactive disease with a good deal of avascular sclerosis. It is interesting that in the first patient (No. 13) where the footplate shows active disease, there was a considerably raised level of plasma growth hormone (59 ng./ml.), whereas in the second patient (No. 15), where the footplate shows inactive otosclerosis, the patient had a low growth hormone level (13 ng./ml.) and his acromegaly was no longer progressive.

Leaving aside the question of otosclerosis, we will now consider the hearing levels of the acromegalic group as a whole, and discuss whether there is any more deafness displayed in this group, than exists in the general population. Fig. 4 shows the degree of hearing loss by air conduction in 30 acromegalic ears, averaged into decade groups. It is evident that the hearing levels in this acromegalic group of patients are substantially lower than those found in the general population by Glorig and others. Now we are presented with the difficult task of trying to establish which particular one of the many features of acromegaly might be responsible for this hearing loss. There are many factors to be considered, including the age of the patient, the duration of the disease, the blood pressure, the

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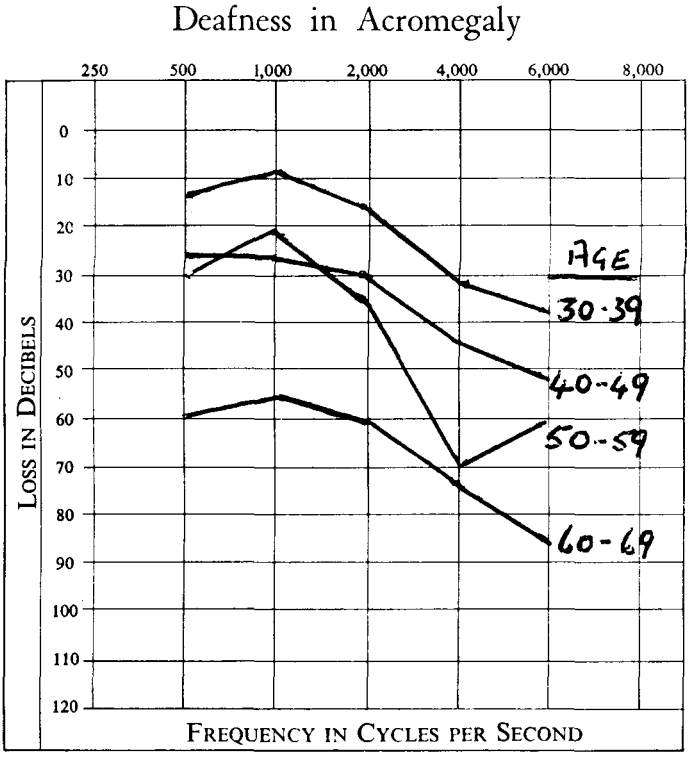


Fig. 4.

Shows the hearing levels in 30 acromegalic ears, expressed as the average loss in each decade group.

diabetes and finally the circulating growth hormone level. In the graphs shown in Figs. 5–8 the degree of deafness is plotted against each one of these variants in turn. In each instance a suggestion of a general trend does emerge, but always the two patients with severe diabetes (marked with a "D") and the three patients with conduction deafness (marked with a "C") do not conform to the general pattern.

Fig. 5 shows the degree of deafness as a function of age. Apart from the reservations already made concerning conduction deafness and diabetes, one can see that, not surprisingly, there is a general tendency for the degree of deafness to increase with age.

Fig. 6 shows the hearing loss as influenced by the patient's blood pressure. As in the question of age, and probably with the same factors at work, one sees the same type of distribution with a tendency to increased hearing loss with increase of blood pressure.

Fig. 7 shows the degree of deafness as a function of the duration of the disease, and here there does not seem to be any relationship at all. This may be because there is no relationship, but equally it may be because it is difficult to discern, with any accuracy, when the onset of

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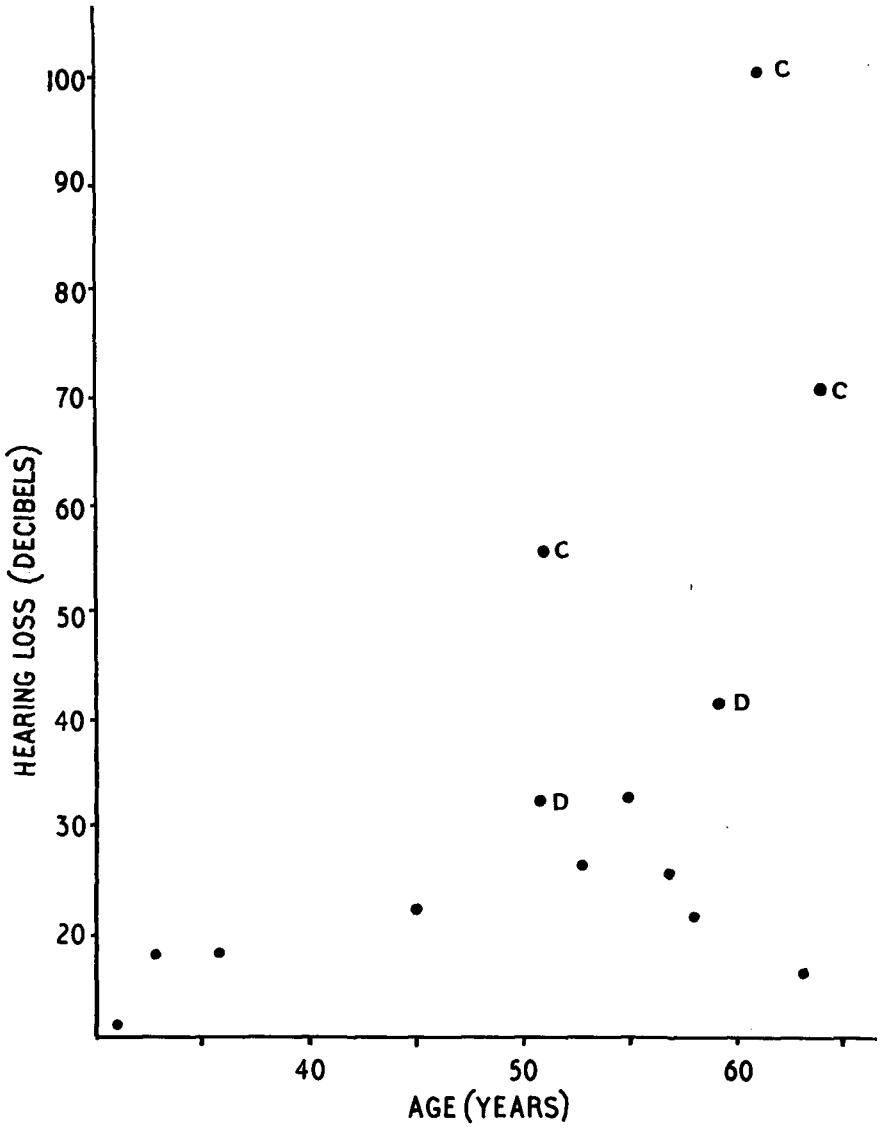


FIG. 5.

Shows the hearing loss by air conduction in 15 acromegalic patients as a function of age. The hearing level is expressed as the average loss in decibels in the two ears at 0·5, 1, 2, and 4 kilocycles. It will be seen that the 3 patients with conduction deafness (marked "C") and the 2 patients with severe diabetes (marked "D") do not conform to the general trend.

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the disease occurred. Acromegaly begins insidiously and may be present for very many years before the patient has symptoms, or before someone notices the characteristic changes in his appearance.

In Fig. 8 deafness is plotted against the patients' plasma growth hormone levels and here again there is no demonstrable direct relation-

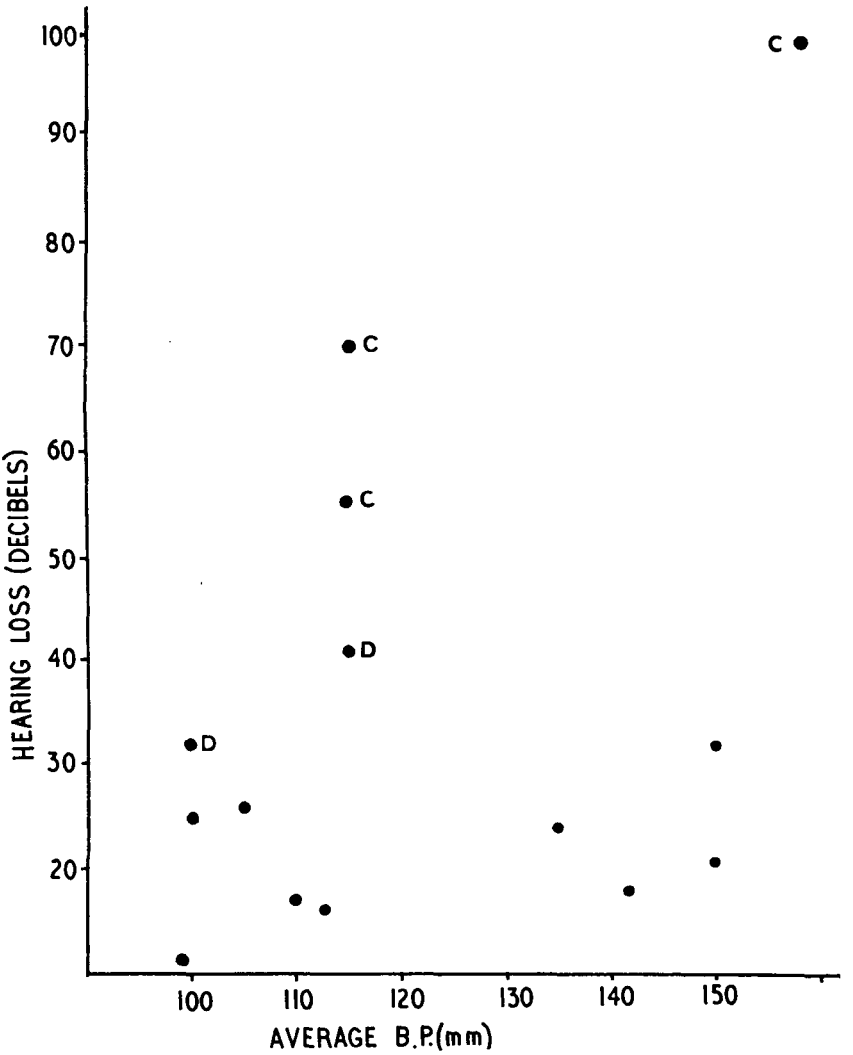


FIG. 6.

Shows the relationship of the average hearing loss in the 15 acromegalic patients studied to the average blood pressure. (Taken as a mean of the systolic and diastolic readings.) The graph shows that there is a tendency for the hearing to be worse in the patients with the higher blood pressure. Again, the patients with conduction deafness and those with severe diabetes do not conform to the trend.

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ship between the two. If anything, the degree of hearing loss seems to be greater in those with low rather than high growth hormone levels. This led us to wonder whether there might not, in fact, be an inverse relationship between the two factors.

In Fig. 9 the hearing level is plotted against the inverse value of

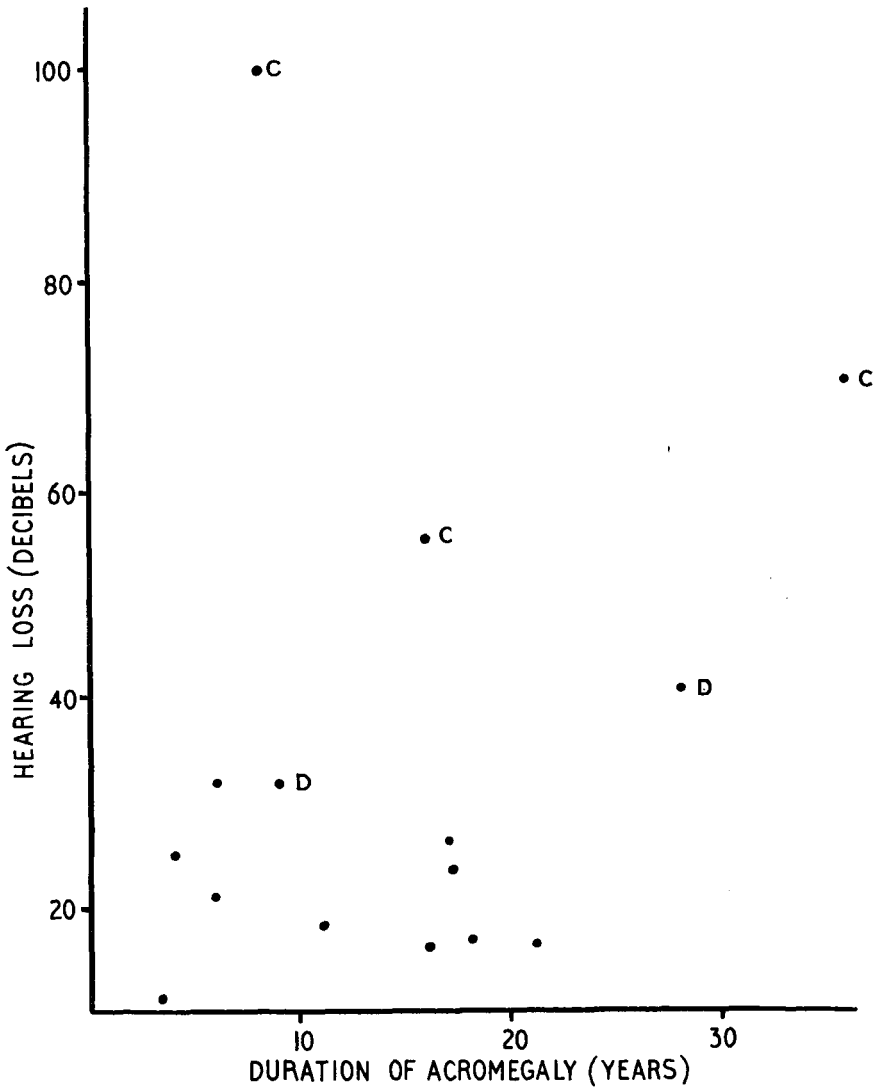


FIG. 7.

Shows the average hearing loss in 15 acromegalic patients plotted against the duration of the acromegaly in years. There is apparently no clear relationship between the two factors.

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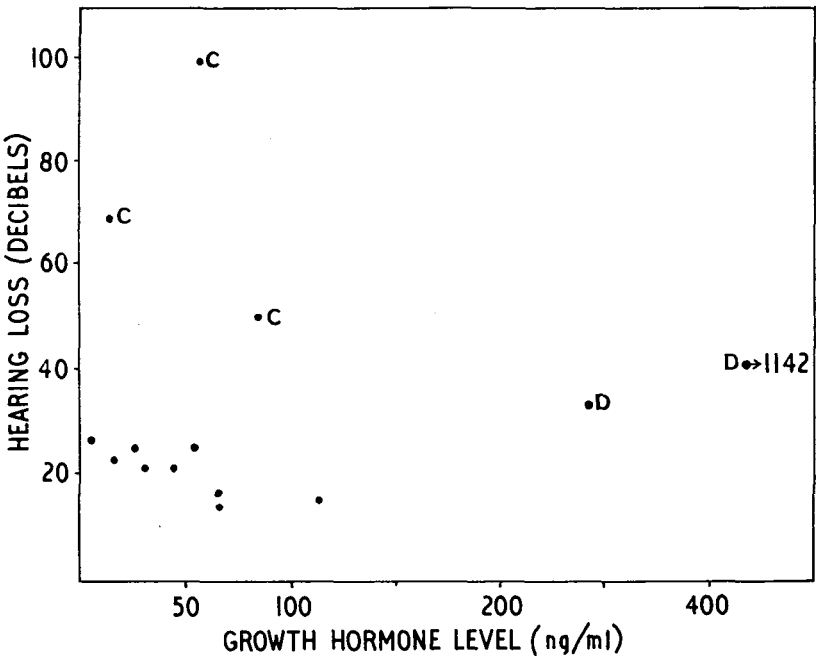


FIG. 8.

Shows the hearing loss in 15 acromegalic patients as a function of growth hormone level. It can be seen that there is no direct relationship.

the growth hormone level. Very interestingly, and rather surprisingly, this graph does show that there is some relationship between the two factors and that the patients with the better hearing are those with the higher hormone levels. This tendency shows more clearly when bone conduction readings are charted, and here the two patients who have a severe conduction defect come more into line with the general trend (Fig. 10).

Conclusions

In attempting to draw conclusions from these results there are three major difficulties.

1. Because acromegaly is a very uncommon disease, any published series must, of necessity, be small and any results obtained will be of questionable statistical significance.

2. Both deafness and otosclerosis are common conditions and will occur in almost any group of patients studied, whether there is any direct relationship or not.

3. Acromegaly affects so many different tissues and biochemical

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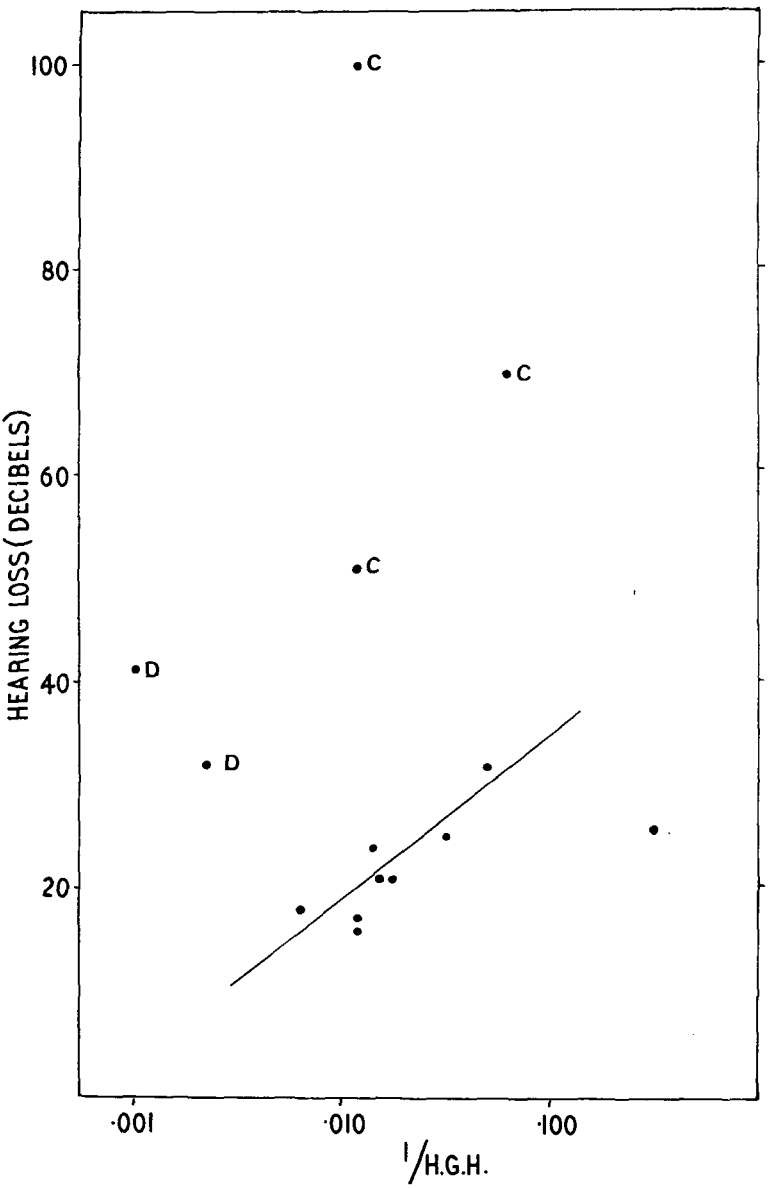


FIG. 9.

Shows the hearing loss in 15 acromegalic patients as a function of the inverse value of the plasma growth hormone level. This graph indicates that the hearing loss is most marked in those patients with a low growth hormone level. The patients with conduction deafness and the severe diabetic patients do not conform to the general trend.

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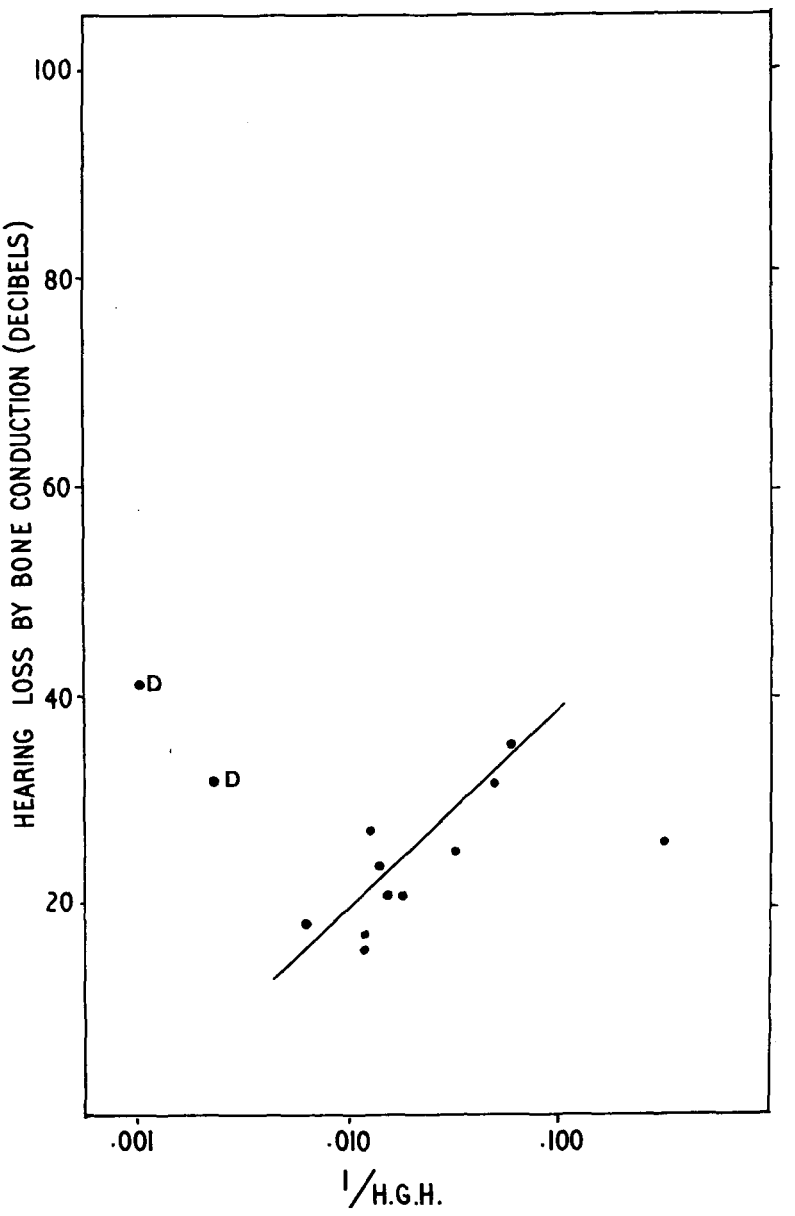


FIG. 10.

Shows the hearing level by bone conduction in 15 acromegalic patients as a function of the inverse value of the plasma growth hormone level. The trend shown in FIG. 9 is now more marked. The 2 patients with severe diabetes (marked "D") again do not conform to the general trend.

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mechanisms that it is very difficult to isolate and study any one factor that might be responsible for changes in the temporal bone.

However, in these 30 acromegalic ears, a significantly increased incidence of deafness has been demonstrated, and five of them showed a marked conductive loss. The diagnosis of otosclerosis involving the footplate has been histologically confirmed in two of them and there is strong presumptive evidence that the other three are similarly affected. All the ears showed some degree of perceptive deafness, but there is no direct evidence to show that this is due to cochlear otosclerosis, though this might well be the case. There is apparently no direct relationship between the level of circulating growth hormone and the degree of deafness, but there is evidence to indicate that the degree of deafness tends to increase as the growth hormone level falls off. This is not as surprising as it at first appears, because, after all, the onset of otosclerosis occurs in normal people at an age after normal growth has ceased. Similarly the increased deafness of otosclerotic patients in association with pregnancy tends to occur after parturition when the level of circulating growth hormone is falling, rather than during the pregnancy when it is high. Barton studied the effect of pregnancy on otosclerotic deafness and found that of those who were further deafened by childbearing, only 20 per cent. suffered deterioration during the actual pregnancy. The other 80 per cent. experienced deterioration during the 6 months after childbirth. Simson Hall maintains that it is during the healing or sclerotic phase of otosclerotic activity, that deafness occurs. It may well be that this sclerotic or healing process takes place in the temporal bones of acromegalic patients, when the circulating growth hormone level falls. To date, only 7 of our acromegalics have had a trans-sphenoidal hypophysectomy and the results of their subsequent growth hormone assay are not yet available. It will be of great interest to see what happens to their hearing levels during the first few years after operation.

Summary

The hearing levels in a group of 15 patients suffering from acromegaly were evaluated. Out of 30 ears studied, 5 were found to be otosclerotic and all suffered from varying degrees of perceptive deafness. It was found that there was no direct relationship between the level of circulating growth hormone and the level of cochlear function, but the results appear to indicate that the hearing is worse in those patients with the lower levels of circulating growth hormone.

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REFERENCES

BARTON, R. T. (1945) *New Engl. J. Med.*, **233,** 433.
CAWTHORNE, T. E. (1947) *Proc. roy. Soc. Med.*, **40,** 168.
ESCAT, E. (1922) Surdites progressives et otospongiose' Part 2. Monographies Oto-rhino-laryngologiques Internationales, No. 7.
GLICK, S. M., ROTH, J., YALOW, R. S., and BERSON, S. A. (1963) *Nature (Lond.)*, **199,** 784.
GLORIG, A., and GALLO, R. (1962) *In* Otosclerosis. Henry Ford Hospital International Symposium, edited by H. F. Schucknecht. Boston and London, p. 63.
GREENWOOD, F. C., STEWART, H. J., FORREST, A. P. M., and WOOD, R. G. (1965) *Lancet*, **2,** 555.
HUNTER, W. M., and GREENWOOD, F. C. (1964) *Biochem. J.*, **91,** 43.
MENZEL, O. J. (1966) *Eye, ear, nose thr. monthly*, **45,** no. 8, p. 84.
NAGER, F. R. (1933) *Z. Hals-, Nas-u-Ohrenheilk.*, **34,** 72.
RABEN, M. S. (1962) *New Engl. J. Med.*, **266,** 31.

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