DEAFNESS IN HYPOTHYROIDISM

By J. A. De VOS (Bruges)*

In this communication a survey has been made of the hearing capacity of a number of patients suffering from acquired hypothyroidism. A parallel experimental investigation has been made in which hypothyroidism was induced in several species of small mammals by the addition of propyl-thio-uracil to their diet. Histological examination of the thyroid gland and of the inner ear was carried out and the results are set out below.

Hypothyroidism has been recognized since the Hippocratic age (Siegel, 1960), but the association of loss of hearing with this condition has only been appreciated since the end of the nineteenth century.

Hypothyroidism can be divided into two main groups:

(i) Congenital hypothyroidism.

(ii) Acquired hypothyroidism.

Congenital Hypothyroidism

This condition is encountered in *sporadic cretinism*—goitrous or non-goitrous—and to some degree in endemic cretinism. While the sporadic goitrous cretinism is clearly an inherited condition and is caused by a congenital enzymatic defect in the thyroid gland, the sporadic non-goitrous cretinism or athyreotic cretinism consists of failure of the thyroid gland to develop in fœtal life. Both these conditions cause hypothyroidism and an adequate replacement therapy can successfully reverse the pathological changes involved. The anatomical changes in the auditory apparatus in endemic cretinism are set out below.

These changes according to de Quervain and Wegelin (1936) do not occur in congenital athyreosis. Moreover deafmutism does not occur in sporadic cretinism. Hypothyroidism was also encountered to some degree in *endemic cretinism*. Numerous studies were carried out upon these cases of endemic cretinism in the early years of this century with special reference to the associated deafmutism. Congenital deafness occurring in cretins was fully discussed by Siebenmann (1902, 1904, 1912), who recorded that there were in Switzerland 24 cases of congenital deafness due to thyroid deficiency per ten thousand of the population. J. S. Fraser

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(1932) quotes Nager as saying that among cretins there are 29 per cent. of deaf mutes and 32 per cent. with hardness of hearing. Fraser also quotes Stein as saying that 25 per cent. of cretins have normal hearing, 45 per cent, have severe deafness and 5 per cent. total deafness.

In their cases there was failure of absorption of myxomatous material in the middle-ear cavity, failure of full development of the ossicles and in some of them there was also a Scheibe type of degeneration of the scala media and the organ of Corti. Originally the immediate cause of these changes was thought to be a deficiency of thyroid secretion.

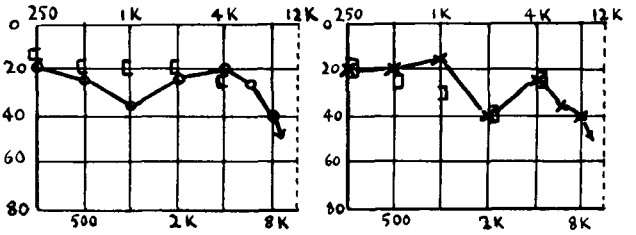
It seems quite clear now after the account of de Quervain and Wegelin (1936) and the more recent one of Raman and Beierwaltes (1959) that only a few of the endemic cretins are hypothyroid whilst deafmutism and hardness of hearing are somewhat common features in this type of disease. Moreover it seems difficult to admit that deafmutism in endemic cretinism should be attributed to hypothyroidism in post-natal life, whilst it does not occur in sporadic cretinism. It could, however, as Trotter (1960) pointed out, be the result of hypothyroidism during fœtal life. Furthermore, the type of audiometric curves found in acquired hypothyroidism does not concord with that of total or sub-total deafness as found in many cases of endemic cretinism and in Pendred's syndrome (1896). In endemic cretinism although the usual curve is that of a perceptive deafness, other curves, especially that of the central type, may be encountered as Gušić pointed out (1957). In the acquired cases of hypothyroidism the lesion causing the deafness appears to lie to the cephalic side of the inner ear, either in the nervous tracks or in the central connections of the cochlea. The audiometric curves are more of the central type, either flat or concave towards the threshold line, and rarely showing the slope away from threshold as the frequency increases. In addition to this there is hardly ever any notable interference with the vestibular function, and this in itself, is against the lesion being located in the peripheral part of the VIIIth nerve. Moreover, two of the 32 cases set out below are examples of what is known as *Pendred's syndrome*, which is a congenital deafness associated with goitre in a district in which goitre is not endemic. The deafness in these cases is of the perceptive type, and shows the congenital curve concave towards the threshold line. The deafness can be total or may be slight. There may also be some reduction of vestibular function.

It has been emphasized that not all these cases of sporadic goitre suffer from hypothyroidism, the greater proportion being euthyroid. In cases of Pendred's syndrome the goitre is the main clinical feature and it could be considered an abnormal response of the thyroid gland to an enzymatic defect, which prevents it from forming organic iodine compounds at a normal rate. In the words of Fraser, Morgans and Trotter (1960) "The deafness is not caused by hypothyroidism, but is an independent expression of the same gene effect".

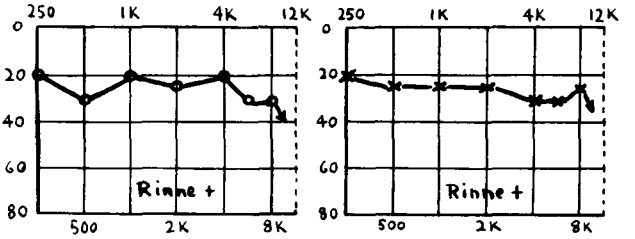
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Acquired Hypothyroidism

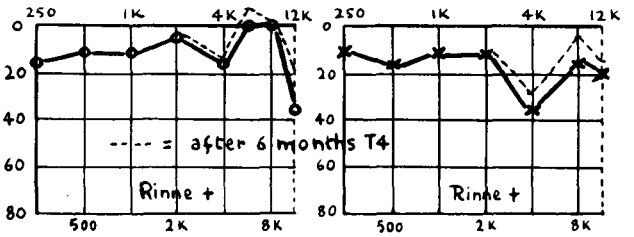
The Myxœdema Committee of the Clinical Society of London found, in 1888, auditory dysfunction in 38 patients out of 69 suffering from myxœdema. More precise surveys about the type of deafness have since then been made. Some authors favour middle-ear deafness, others emphasize the possibility of either a conductive deafness or a perceptive one. In the latter case attention must be drawn, as it has been by Marquet



Case 3.



Case 4.



Case 6.

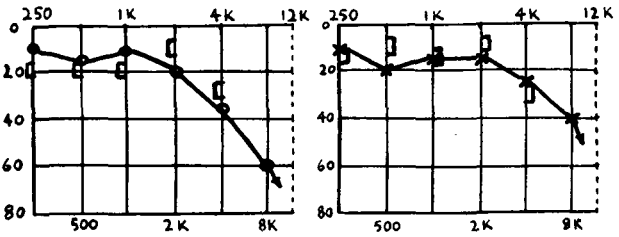
(1956) to the absence of recruitment, which suggests a neural or a central auditory defect. Several authors who described a mixed conductive and perceptive deafness considered that the perceptive element was transitory in nature, while the conductive factor persisted.

A series of patients, attending the Endocrine Clinic at the New End Hospital, London, were examined and observed over a period of six to eight months, by kind permission of Mr. J. E. Piercy and Dr. Raymond Greene. All were suffering from some degree of myxœdema, and were

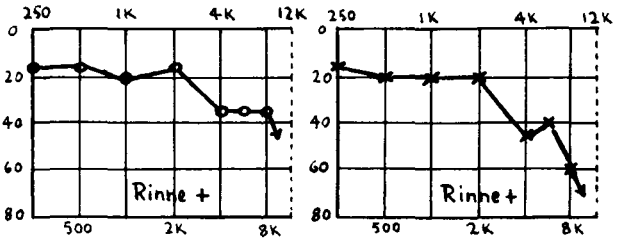
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under investigation and treatment. Their ears were examined and their hearing tested audiometrically. All those who had any history of disease or injury to the ear were discarded and thirty-two were left who had no history or signs of previous ear trouble. Fifteen of these myxœdematous patients had normal hearing.

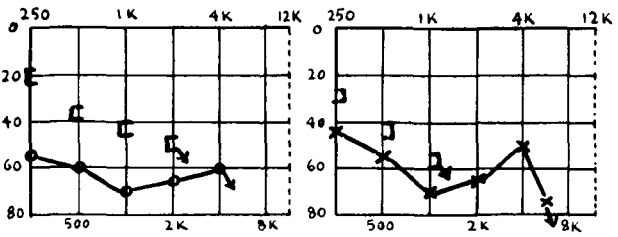
Of the 17 patients with demonstrable hearing loss, two were very severely deafened, one sub-totally, but they were congenital cases of



CASE 8.



CASE 14.



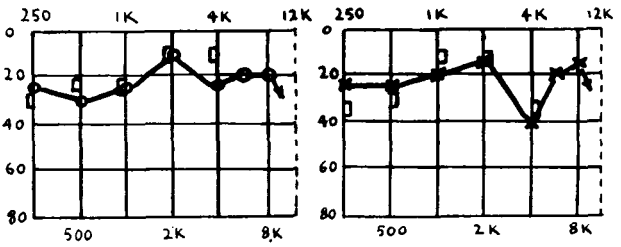
CASE 16.

deafness and were described as examples of Pendred's syndrome. In ten the loss was slight, between 20 and 30 decibels above threshold and the audiometric curves were mainly flat, a number being concave towards the threshold line. In three the deafness was described as moderately severe, due to a more marked degree of loss for the higher frequencies. One had severe deafness in one ear, mainly for the high tones and the final one had severe deafness and also vertigo.

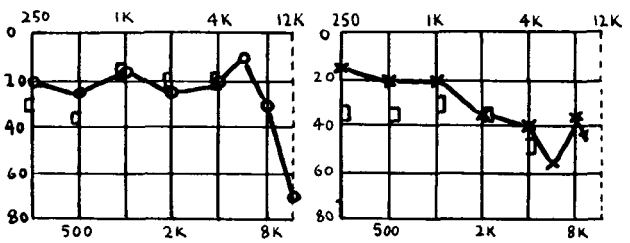
In none of the 32 cases was there any sign of conductive deafness.

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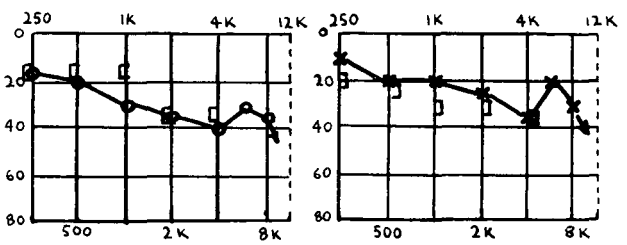
Two patients with myxœdema were seen with pure conductive deafness, but both gave a history of otitis media and otorrhœa, and were, therefore, not included in the present survey. In a number of the cases audiometric controls were repeated over a period of months during which they were undergoing treatment for their myxœdema. Clinically, as far as the thyroid function and the metabolic rate are concerned, they had returned to normal, but there was no improvement in the hearing. It is possible that,



Case 18.



Case 20.



Case 21.

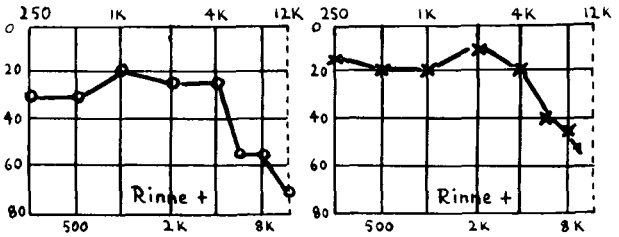
among the patients that have been described with conductive or with mixed deafness, there are some with œdema of the eustachian tube and consequently some conductive deafness. If such patients have thyroxine treatment the œdema may subside, reducing the conductive moiety of the deafness but leaving the permanent neural or central lesion.

Of the audiographs of 12 patients seven (3, 4, 6, 16, 18, 21 and 31) have a flat response curve without marked upper tone loss. These include the two congenital cases with sub-total deafness (16 and 31). The remaining five

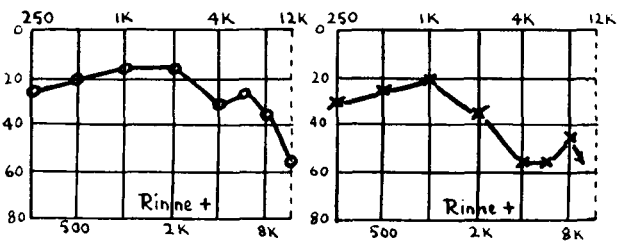
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(8, 14, 20, 27 and 28) show an increased loss of hearing for high tones with normal hearing for the middle and low tones and are suggestive of nerve involvement.

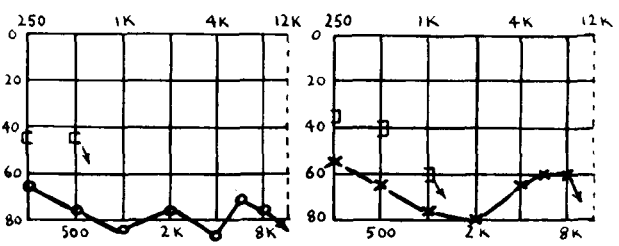
All the patients in this series had deafness which was approximately equal on the two sides, which made the Fowler loudness balance test inapplicable. The test for determination of fatigue phenomenon and a modified Békésy audiometry for registering variation in limen differences were



Case 27.



Case 28.



Case 31.

used. These tests indicated, in all the cases to which they were applied, that there was no abnormal fatigue and that the intensity limen difference was not excessively small in any of the patients. These results indicate a lack of recruitment and confirm those reported by Marquet (1956). Lack of recruitment appears to rule out the end organ as the site of the lesion and points rather to a neural or to a central location. Some caution is needed, however, in the interpretation of these tests as recruitment is possible in the absence of abnormal fatigue. Inhibition of auditory fatigue and the

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Case	Patient	Sex	Age	Clinical history	Cholesterol	B.M.R.	Urinary excretion total† 0·8 hrs., 8·24 hrs., 24-48 hrs.	T index°	PB ^{127}I	T_3 uptake‡	Various tests	Hearing	Dizziness	Remarks
1	M.S.	F.	17	Clinical symptoms of myxœdema for 2 years	494	−30	68	**1·9**	<1	19	Thyr. precipit. (−) Thyr. latex fixat. (−)	borderline normal	—	—
2	L.W.	F.	24	Clinically slight myxœdema for 6 months	—	—	94	1·3	3	14	—	Borderline normal	—	Borderline between the normal and the hypothyroid range
3	B.S.	F.	58	*Myxœdema for 6 months*(post I^{131} therapy)	—	—	*70*	2·5	1·9	—	—	*Slight perceptive* deafness	—	—
4	W.D.	F.	56	Myœdema for 28 years (underdosed)	—	−18 −25	—	—	<1	20·2	—	Subnormal	+	—
5	F.R.	F.	33	Cretinism diagnosed at 5 months old	—	−35	—	—	—	—	—	Very slight perceptive deafness	—	R. tymp. scarred
6	E.E.	F.	40	Post-operative myxœdema 20 years ago	303	−17 −17	—	—	—	11·4 21·8*	17 keto: 7·5 mg./24 hrs. 17OH: 6·8 mg./24 hrs. 17 keto: 7·4* 17 OH: 9·6	Dipon 4,000 * slight improvement	—	*=after 5 months' treatment with L-T_4
7	W.M.	F.	68	Clinically hypothyroid	520	+1	75·5	—	—	—	I^{131} neck uptake: 2·8%	Normal	+	—
8	M.D.	F	58	Myxœdema for 10 years (post-thyroidectomy)	364	—	65 (40-20-5)	3·1	—	14·3	—	Perceptive deafness R < L (subnormal)	—	—

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Case	Patient	Sex	Age	Clinical history	Cholesterol	B.M.R.	Urinary excretion total† 0·8 hrs., 8·24 hrs., 24·48 hrs.	T index°	PB ^{127}I	T_3 up take‡	Various tests	Hearing	Dizziness	Remarks
9	D.B.	F.	60	Clinically slightly hypothyroid	328	—	—	—	—	—	—	Normal	—	—
10	R.	F.	(50)	Clinically hypothyroid	401	—	—	—	—	—	—	Normal	+	Dizzy if she does not take T4
11	D.R.	M.	35	Post-operative hypothyroidism	—	—	65 (39·21·4·6)	—	3·3	< 14·5	—	Normal	—	Just in the hypothyroid range
12	H.E.	F.	40	Goitre for 15 years, 3 years œdema	—	—	—	—	—	20*	Immediate uptake: S:I. 0*	Slight to moderate perceptive deafness unimproved*	—	* = after treatment
13	L.F.	F.	52	Thyroidectomy (1953) myxœdema (all clinical symptoms) for 2½ years	—	—	64 (35·21·8)	2·8	—	17 7	Thyr. precipit. (—) Latex fixat. (—)	Normal	—	—
14	E.A.	F.	51	Clinic. hypothyroid for 1 year	—	—	84 (48·30·6)	1·9	—	—	17-keto: 7·4/ 24 hrs. 17-OH: 9·3/ 24 hrs.	Slight to moderate perceptive deafness	—	Untreated before examination
15	M.S.	M.	9	Cretinism diagnosed at 6 wks.; underdosed for years	—	—	—	—	—	—	—	Low normal side (20-35 dB)	—	—
16	R.G.	F.	20	1958: Part. Thyroidectomy 1961: Total thyroidectomy (*follicular* carcinoma)	400	—	73 (47·21·4)	—	—	—	Neck uptake (48 hrs.) 20%	Congenital deafness	—	Pendred's syndrome

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Case	Patient	Sex	Age	Clinical history	Cholesterol	B.M.R.	Urinary excretion total† 0·8 hrs., 8·24 hrs., 24-48 hrs.	T index°	PB ^{127}I	T_3 uptake‡	Various tests	Hearing	Dizziness	Remarks
17	W.E.	F.	59	Clinically hypothyroid for 3 yrs.	425	−28	—	—	—	—	Water diuresis test: 67%	Severe perceptive deafness	*	* improved with T_4 2·5 mg.
18	B.A.	M.	31	Underdosed infantile hypothyroidism. Thyroidectomy for goitre 17 yrs. ago	—	—	—	—	—	—	—	Slight perceptive deafness	—	Received before attendance 0·33 gr. t.d.s.
19	B.R.	M.	16	No clinical symptoms	156	−10 −26 −20	3·3%	—	2 4·4*	16·3	I^{131} i.v. trapped: 23% in the first 9 min. 75% within 25 min.	Normal	—	* after 1 month 50 μg T_3 daily
20	L.L.	F.	48	Clinically myxœdematous for 2 yrs./ goitre 25 yrs. ago	—	—	—	—	<1	11·7	—	Perceptive deafness	—	Untreated before
21	P.M.	F.	42	4 yrs. ago/ partial thyroidectomy (lymphadenoid changes). Clinic. sympt. of myxœd. 6 mths. ago	—	−24 ·32	91 (44·42·5)	—	<1	—	E.C.G.: general flattening of T waves	Slight perceptive deafness	—	—
22	N.V.	F.	55	Clinical symptoms for 1 year	—	—	—	—	1·8	0·1	Latex fixat. (+) Thyr. precipit. (—) *Liver tests:* abnormal	Normal	—	Lymphadenoid goitre coming to a stage of myxœdema
23	B.J.	F.	8	Infantile hypothyroidism without myxœdema or cretinism	450	—	58 (33·16·9)	2·5	—	—	—	Normal	—	—
24	J.E.	F.	24	Partial thyroidectomy 5 yrs. ago	—	—	17 (13·2·5·1·5)	30	3·2	12·1	—	Normal	—	—

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Case	Patient	Sex	Age	Clinical history	Cholesterol	B.M.R.	Urinary excretion total† 0·8 hrs., 8·24 hrs., 24·48 hrs.	T index°	PB ^{131}I	T$_4$ uptake‡	Various tests	Hearing	Dizziness	Remarks
25	L.H.	M.	40	No clinical symptoms but fatigue	—	−7 −5 −1	—	5	3·5	—	Immediate uptake S=0·2	Slight to moderate perceptive deafness	—	—
26	S.T.	F.	18	Clinically hypothyroid for 3 yrs.			radio-iodine tests were on the borderline between normal and deficient thyroid function (figures not available)					Normal	—	—
27	C.R.	F.	50	Clinically hypothyroid for 3 yrs.	—	—	75 (42·25·8)	2·2	—	14·2	—	Slight to moderate perceptive deafness; abnormal biauricular integration	—	—
28	J.E.	F.	46	Clinically hypothyroid for 2 yrs.	300	—	—	—	—	13·1	—	Slight to moderate perceptive deafness; normal biauricular integration	+	—
29	M.L.	F.	45	Clinically hypothyroid for 3 yrs.; treated periodically	—	—	—	2·2	3·2	14	—	Normal	—	—
30	L.E.	F.	67	In 1944 thyroidectomy for Graves' disease. Clinically very hypothyroid	—	—	—	—	8·5*	—	—	Normal hearing—tinnitus; normal biauricular integration	+	* after treatment with T_3 (June, 1960)
31	P.M.	M.	14	1959: partial thyroidectomy (fœtal type adenoma + severe epithelial hyperplasia	—	—	24 hrs. excr. 37 (23·14)	—	—	—	Neck scan 24 hrs.: 40%	Congenital deafness	—	Pendred's syndrome
32	S.O.	M.	61	Clinically hypothyroid for 6 yrs.; treated periodically	420	−18	—	—	5*	17·5*	17 keto: 7 mg / 24 hrs. (low)	Normal	—	*—after T4

† Hypothyroid: 55·95 Normal: 25·55 Hyperthyroid: 5·25
° Hypothyroid: 0·3 Normal: 3·13 Hyperthyroid: over 20
‡ Hypothyroid: <14·5 Normal: 15·20 Hyperthyroid: >20

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bi-auricular integration were tested in three of these cases by the method of Maspetiol, Semette and Mathieu (1960-61), in only one of which was the result abnormal. From this short series it is difficult to make a definite decision on the probability of a central localization of the lesion. Although the possibility of involvement of the middle ear in myxœdema is not denied it seems that the preponderant lesion must be localized in the neural auditory apparatus.

Lindsay (1942) refers to attacks of vertigo where the basal metabolic rate is lowered and where the blood pressure is also reduced. In the 32 cases in this series vertigo was experienced by six patients only. Of these six the hearing was normal in three (7, 10 and 30), there was severe perceptive deafness in one (17) and in the remaining two there was a slight perceptive deafness. One of these had a flat audiometric curve at 20-30 decibels above threshold (4), the other had an upper tone loss on one side and 4096 dip on the other side (28). In two of these patients suffering from vertigo, in whom the bi-auricular integration test was carried out, the result was normal. The only patient of the series who showed an abnormal integration had no vertigo.

Reviewing the 32 cases of myxœdema with 17 examples of perceptive deafness and of vertigo, there does not appear to be any factor in the thyroid or in the general condition which leads to the emergence of these two symptoms of involvement of the ear. Congenital or acquired post-operative, mild or advanced hypothyroidism are equally present in these cases, whether they have or do not have aural complications and these complications appear to be entirely sporadic.

Pathology of the Inner Ear in Hypothyroidism

In 1909 the auditory apparatus of three human cretins and one animal cretin was studied by G. Alexander. Briefly the following features were found: degeneration of the saccular macula, thickening of the basilar membrane, hypoplasia or atrophy of the *stria vascularis* and the spiral ganglion. He also described a partial degeneration of the sensory cells of Corti. The same year J. Haberman (1909) investigating two cretins, did not find any characteristics which were suggestive of a lesion of the inner ear. An account of this problem has also been published by P. Manasse (1909). In three cases of total deafness with goitre (two deaf mutes) he described various anomalies of the osseous labyrinth which he considered as being congenital. Furthermore he described various involvements of the membranous labyrinth of which the most striking were—degeneration of the tectorial membrane and of the organ of Corti, with absence of the pillars and tunnel, with thickening of the basilar membrane and with degenerative changes in the cochlear nerve and spiral ganglion. He does not consider these malformations congenital. More accounts on this subject

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have been published and were summarized in a recent communication (Ormerod, 1960).

Information is not yet available about the pathology of the ear in either Pendred's syndrome or in human myxœdema. Very few studies have been made on experimental animals. At the time of going to press, only the experiments of Ritter and Lawrence (1960) on chicken embryos have been published. They found general changes in embryos to which thiourea had been administered on the fourth day of incubation. In the surviving chicks there was underdevelopment and delayed hatching. In the organ of Corti they found œdema in the region of the nerve cells of the acoustic papilla.

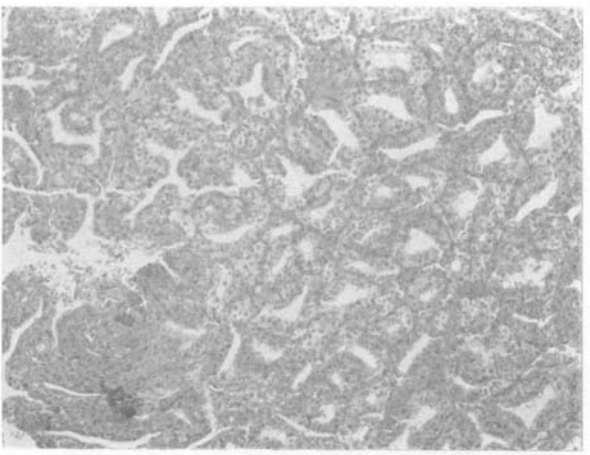


FIG. 1.

Thyroid gland of a mouse after 6 weeks on propyl-thio-uracil, slight degree of hyperplasia. ×120.

As the lagena of birds is very different from the mammalian cochlea it was felt advisable to carry out the experimental study upon those of the rat, the mouse and the hamster. Mice used in these experiments were white mice which, because of their free breeding, were readily available. They are not as suitable as the normal coloured mice because the labyrinth in the white mouse, even when functioning normally, is not so well shaped or formed, and there tends to be a higher proportion of cochlear degeneration and deafness among them. The various abnormal animals such as waltzing, shaker and zig-zag mice and other similar animals were not used because of the hereditary lesions in the labyrinths of these mice. (Grüneberg, *et al.*, 1940), (Grüneberg, 1956). Propyl-thio-uracil was administered to the animals directly after birth by adding a solution of 0·1 per cent. Propyl-thio-uracil in 5 per cent. sucrose solution to the drinking water for a period of 6 weeks to 21 weeks. Propyl-thio-uracil

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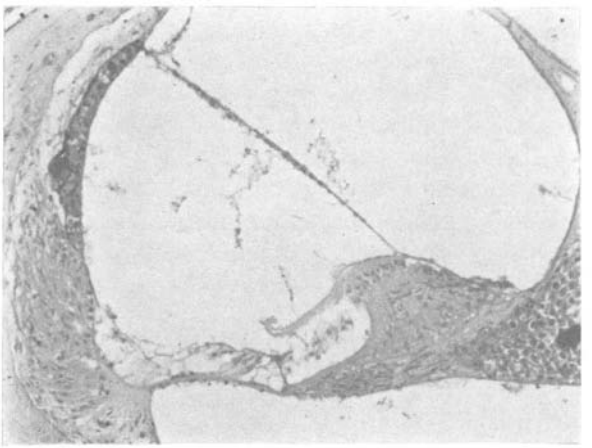


FIG. 2.
Normal inner ear of mouse. ×150.

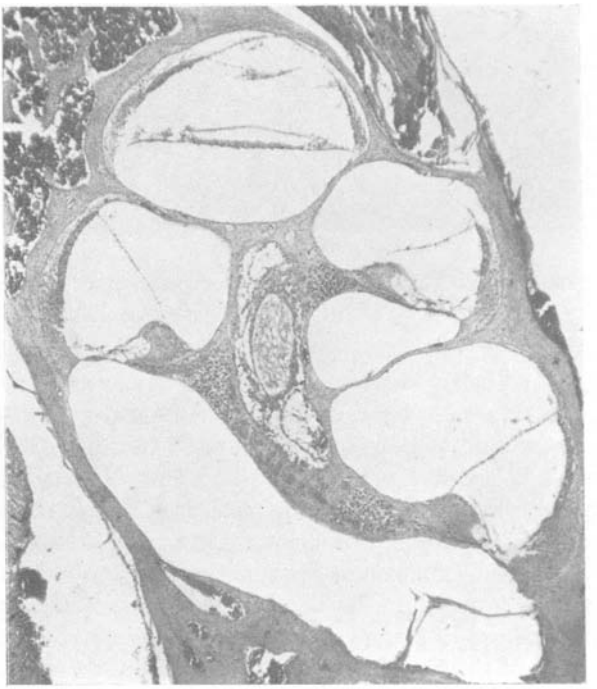


FIG. 3.
.er ear of mouse after 6 weeks on propyl-thio-uracil, slight degeneration of spiral ganglion.
×45.

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inhibits the formation of organic iodine while inorganic iodide is still able to enter the thyroid (Iino, *et al.*, 1961). In order to observe further an eventual reversibility of the lesions obtained, a few animals were returned

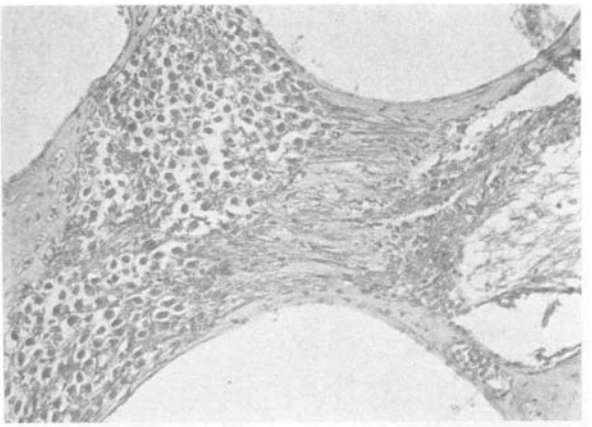


FIG. 4.
Inner ear of mouse after 6 weeks on propyl-thio-uracil, spiral ganglion shows slight degeneration, higher magnification. ×224.

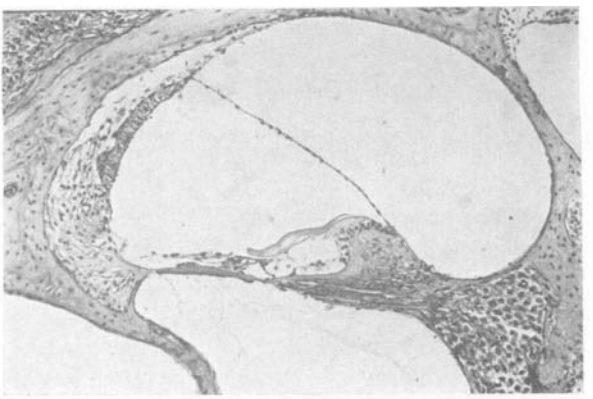


FIG. 5.
Inner ear of mouse after 3 months on propyl-thio-uracil, slight degeneration of cochlear nerve and spiral ganglion, thickening of basilar membrane. ×160.

to a normal diet after having received Propyl-thio-uracil for varying periods. The temporal bones were placed in formol saline, decalcified, double embedded in celloidin and paraffin wax and stained with hæmatoxylin and eosin.

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Experimental Results

A. The Mouse

(*a*) *After 6 or 7 weeks Propyl-thio-uracil*

(i) *Thyroid* macroscopically much enlarged. Microscopically there was already a high degree of hyperplasia (Fig. 1).

(ii) *Inner ear*—one mouse out of two different batches—each showed a very slight degeneration of the spiral ganglion (Figs. 3 and 4). (See Fig. 2 for inner ear of normal mouse.)

(*b*) *After 3 months on Propyl-thio-uracil*

Slight degeneration of the nerve and the spiral ganglion. Thickening of the basilar membrane (Figs. 5 and 6).

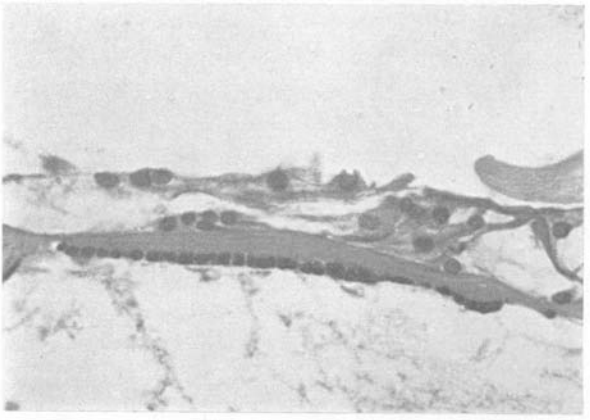


Fig. 6.

Mouse after 3 months on propyl-thio-uracil, thickening of basilar membrane, higher magnification of Fig. 5. ×720.

(*c*) *After 5 months on Propyl-thio-uracil*

No changes in the nerve (Fig. 7).

(*d*) *After 6 weeks on Propyl-thio-uracil and subsequently 14 weeks on normal diet*

(i) Thyroid macroscopically back to normal size.

(ii) *Inner ear*—no changes in the nerve or inner ear (Figs. 8a and 8b).

B. The Rat. It has been established that in white rats the period of the second and third month corresponds to that of maximum increase of metabolism (Litovchenko, 1941).

(*a*) *After 9 weeks on Propyl-thio-uracil*

Two animals were examined. Macroscopically the thyroids were much enlarged, and histological examination showed slight hyperplasia (Fig. 9). There were no demonstrable changes in the inner ears (Fig. 10 inner ear of normal rat).

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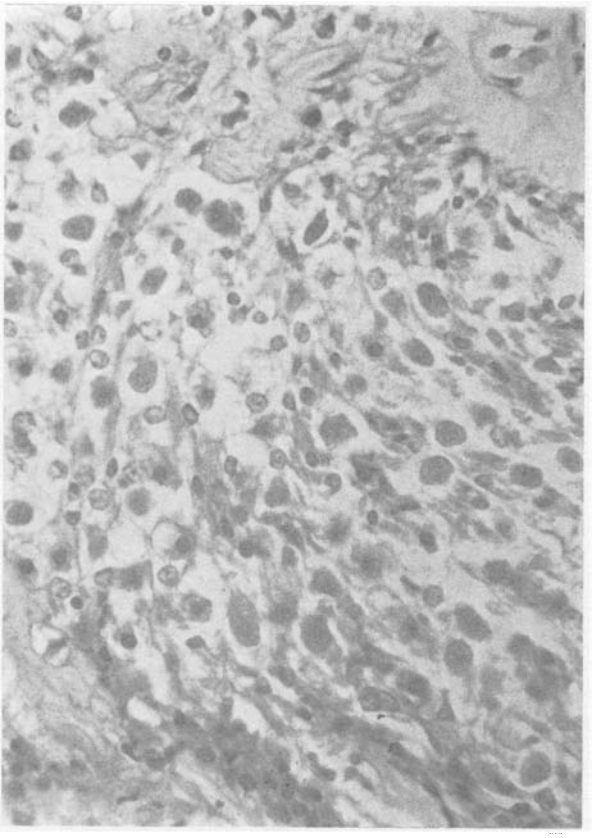


FIG. 7.
Mouse after 20 weeks on propyl-thio-uracil, no change in nerve. ×520.

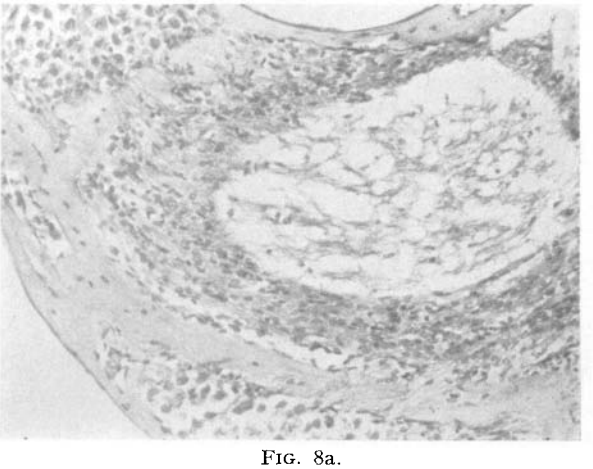


FIG. 8a.
Mouse after 6 weeks on propyl-thio-uracil and subsequently 14 weeks on normal diet, no change in nerve. ×256.

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(*b*) *After 4 months on Propyl-thio-uracil*

Two animals were examined—thyroid gland was much enlarged and, histologically, showed hyperplasia (Fig. 11, upper part and Fig. 12—higher magnification). The inner ear showed degeneration of the spiral ganglion (Fig. 13).

(*c*) *After 2 months on Propyl-thio-uracil, followed by 6 weeks on normal diet*

Three animals examined—

(i) Thyroid back to normal size. Histology showed vesicles containing colloid (Fig. 11, lower part).

Inner ear—normal.

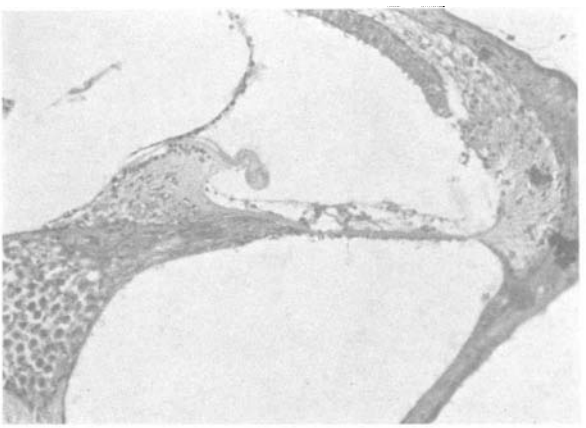


FIG. 8b.

Mouse after 6 weeks on propyl-thio-uracil and subsequently 14 weeks on normal diet. No change in inner ear. ×208.

C. THE HAMSTER

After 5 months on Propyl-thio-uracil

Three animals were examined—

(i) Thyroid gland was very much enlarged. Hyperplasia was present (Fig. 14).

(ii) Inner ear showed slight degeneration of the spiral ganglion with a normal organ of Corti (Fig. 15).

Conclusions

The foregoing experiments have shown that the organ of Corti was not morphologically changed in acquired hypothyroidism, the only anatomical lesion found being a slight degeneration of the spiral ganglion. This degeneration was generally, but not always present. Although the thyroid tended to recover its normal characteristics both histologically and macroscopically when propyl-thio-uracil was stopped, it has not been

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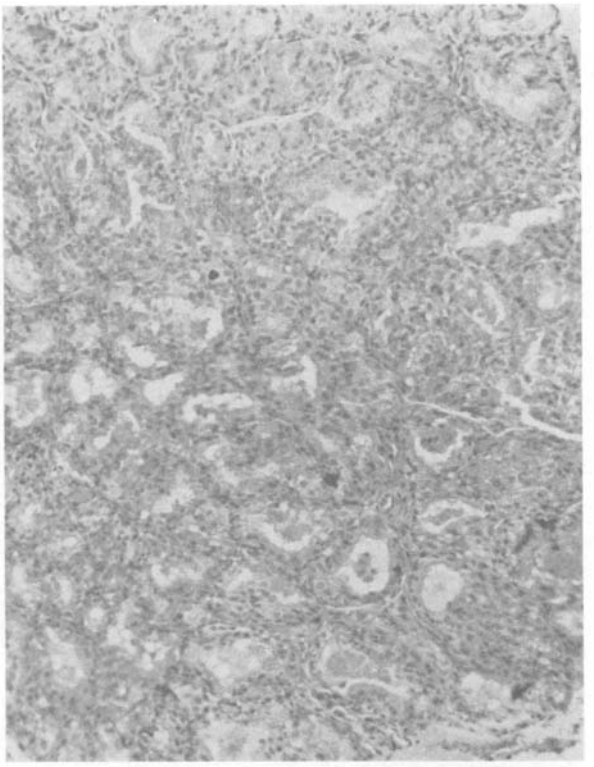


FIG. 9.
Rat after 9 weeks on propyl-thio-uracil, slight hyperplasia of thyroid gland. ×120.

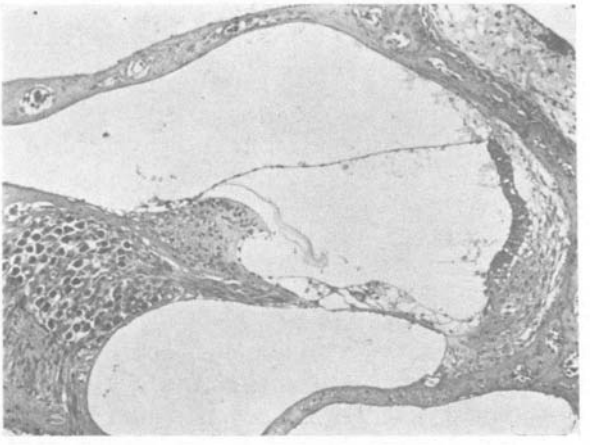


FIG. 10.
Rat after 9 weeks on propyl-thio-uracil, no changes in inner ear or in nerve or spiral ganglion. ×90.

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possible for technical reasons to demonstrate that the degeneration in the ganglion remained unchanged as would be expected. However one has to be very careful in assessing experimental results in animals and applying them to human dysfunctions.

The changes observed seem also to confirm the discordance found between the pathological changes of myxœdema and those in endemic

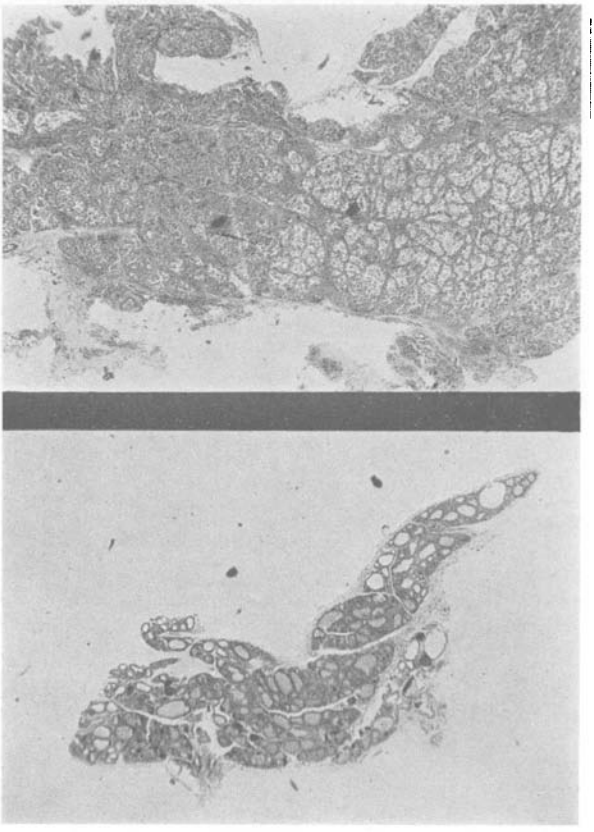


FIG. 11.
Upper section. Rat after 16 weeks on propyl-thio-uracil, Thyroid gland shows hyperplasia. ×25.
Lower section. Rat after 8 weeks on above treatment followed by 6 weeks on normal diet: return of thyroid gland to normal. ×25.

cretinism which were well described by Siebenmann (1902, 1904, 1912) as being deformities mainly in the middle ear. The degree of deafness also makes a distinction between myxœdema and endemic cretinism where the deafness is often severe. For the experiments have shown that the relative lack of pathological changes in the cochlea conform with the mild degree of deafness which is present in rather more than half the patients suffering from myxœdema. This has furthermore been emphasized

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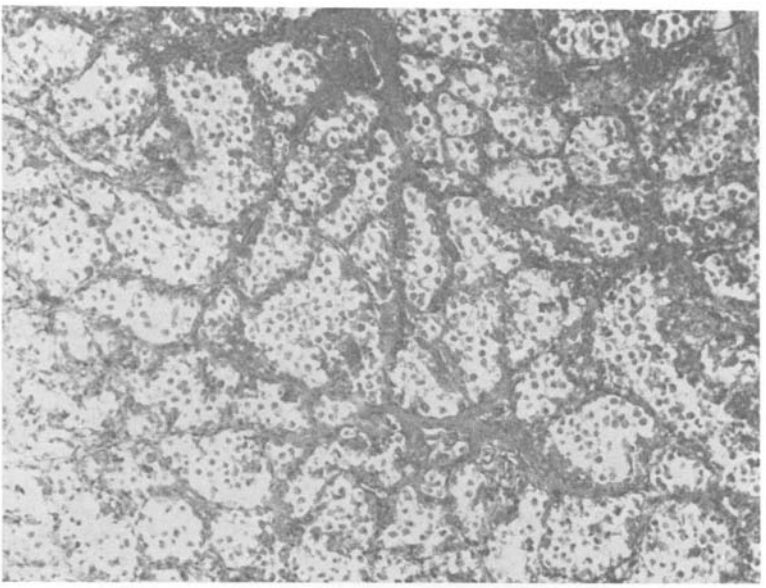


FIG. 12.
Same section as in Fig. 11 upper part. Hyperplasia of thyroid gland higher magnification. × 100.

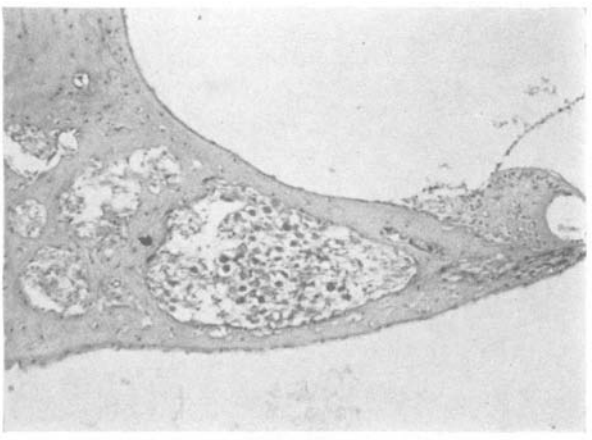


FIG. 13.
Rat after 9 weeks on propyl-thio-uracil. Inner ear, degeneration of spiral ganglion × 140.

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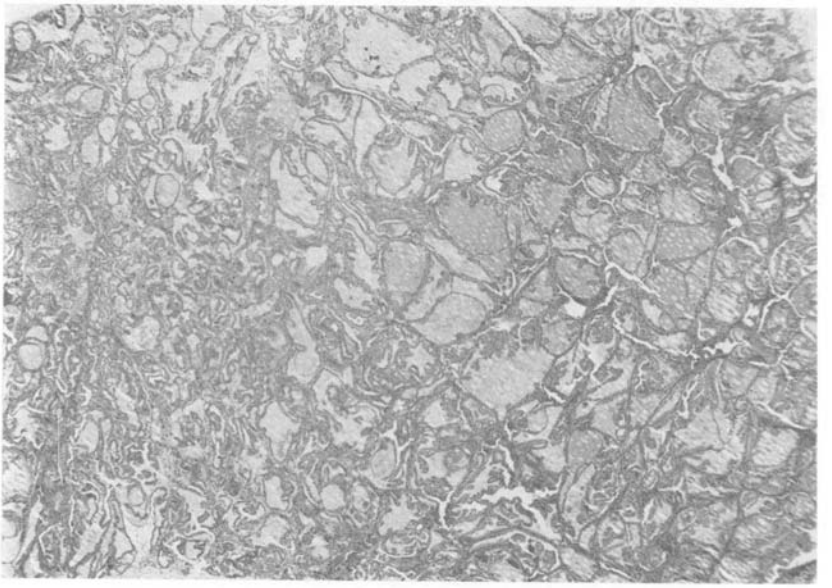


FIG. 14.
Hamster after 21 weeks on propyl-thio-uracil, hyperplasia of enlarged thyroid gland. ×25.

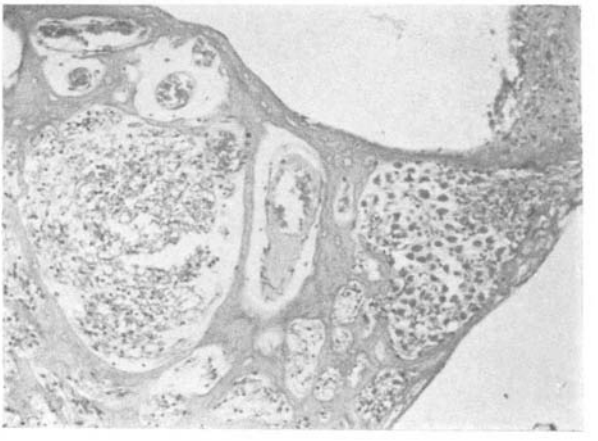


FIG. 15.
Hamster after 21 weeks on propyl-thio-uracil, degeneration of spiral ganglion (no change in organ of Corti). ×170.

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by Schuknecht (1955), Elliott (1961) and others. They stated that the degree of hearing loss is related to the particular structure involved in the inner ear, to its degree of involvement and to its range. The absence of changes in the cochlea, the degeneration of the spiral ganglion, the absence of recruitment with the perceptive type of deafness and the more various types of audiometric curves obtained (Gušić, 1957) favour a nervous or a central involvement of the auditory pathways.

Little can be said about the relationship with the central nervous system as there is still no agreement about the various methods of testing this central deafness.

It seems quite clear after these findings that the pathology of acquired hypothyroidism is radically different to that of endemic cretinism and Pendred's syndrome, the latter syndrome being more or less comparable with endemic cretinism. One is certainly tempted to say that in these two pathological entities hypo-thyroidism cannot have a preponderance rôle in the causation of deafness as it is itself often absent. It could, however, be possible—as has been suggested by Trotter (1960)—that there might be a substance circulating in the body which could have a harmful effect on the enzyme-reaction of both the auditory system and the thyroid gland. The formation of this substance could be due to environmental factors in endemic cretinism or to hereditary influences in Pendred's syndrome. It seems equally obvious that the stage of development at which this harmful influence is active—whether in fœtal or in post-natal life—and its duration are of the utmost importance in the incidence of, and the degree of involvement in the degenerative process of both the ear and the thyroid gland.

Appendix

Notes on the tests for hypothyroidism referred to in the tables.

By Raymond Greene

Cholesterol Level

The accepted levels of healthy individuals are 150 to 300 mg. per 100 ml. of blood. Many circumstances may influence the level and a high one cannot be accepted *per se* as evidence of thyroid deficiency or a normal one as evidence of thyroid normality. Nevertheless as *contributory* evidence of thyroid deficiency, levels above 300 mg. may be accepted in the absence of other causes for a high level.

Basal Metabolic Rate

High levels are suspect but low levels may be regarded as good evidence of thyroid deficiency in the absence of other causes.

Urinary Excretion of Iodine

Total excretions at 48 hours of 55-95 per cent. of the administered dose of ^{131}I. are acceptable as evidence of thyroid deficiency but are not pathognomonic.

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T Index (Thyroid Index)

This index refers to the test devised by Russell Fraser. It is based on the excretion of radioactive iodine after administration of 10μc, in the first 8 hours, the succeeding 16 hours and the next 24 hours, according to the formula $T = \frac{0 \text{ to } 8 \times 100}{0 \text{ to } 48 \times 8 \text{ to } 24}$

It is an excellent screening test for hypothyroidism, normal levels being 3-13.

P.B. ^{127}I (Protein bound Iodine)

The blood level of protein-bound iodine. This is a difficult test to perform accurately, but in good hands is an excellent test of thyroid efficiency in both hypothyroidism and hyperthyroidism when interpreted in the light of clinical findings. The normal levels are 3·5 to 7·5 mg. per 100 ml.

T^3 *Uptake* (Triiodothyronine)

This test measures the amount of thyroxine-binding protein unused by endogenous thyroxine, and is therefore an index of the level of the latter. It is when other circumstances altering the level of thyroxine-binding protein are taken into consideration, an excellent criterion of the level of circulating thyroxine and is probably the best test for distinguishing between the euthyroid and hypothyroid states.

Immunological tests are used to indicate the presence of auto-immune reactions in the thyroid gland. The tests are usually positive in Hashimoto's disease (which always leads to hypothyroidism). They are often positive in hypothyroidism without the typical clinical findings of Hashimoto's disease, and occasionally in other thyroid disorders.

Neck Uptake of ^{131}I

This is still the subject of controversy, but it is generally agreed that the popular "24-hour uptake test" is unreliable. The immediate uptake test of Farran (S) is an excellent way of distinguishing between the hyperthyroid and euthyroid states but far less valuable at the lower end of the normal scale.

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Much of the clinical part of this work has been carried out at the Thyroid Unit of the Endocrine Department, New End Hospital, Hampstead. The author is most grateful to Mr. J. E. Piercy and to Dr. Raymond Greene, and to their staff at New End for their kind permission to study their patients and for their advice and criticism. He is further indebted to Dr. Raymond Greene who has contributed a short appendix in which the various tests for hypothyroidism are described. Some cases of myxœdema were studied at the Hammersmith Hospital, London Postgraduate Medical School, but of these, Cases VII and XVII only are

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reviewed in this account. Professor Russell Fraser has kindly supplied useful information and assistance regarding these patients.

The author wishes to acknowledge his indebtedness to Professor F. C. Ormerod for the opportunity of working in the research laboratories of the Institute of Laryngology and Otology and for his help and advice and to Mrs. Ade Pye who prepared and cut serial sections of the temporal bones and thyroid glands of a large number of animals and who carried out the necessary microphotography.

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