HEART BLOCK IN TOXIC GOITRE.

A Report of Two Cases.

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Auricular fibrillation is a relatively frequent development in cases of toxic goitre, and in this possibly lies the clue to the scant attention paid to the other abnormalities of cardiac rhythm and action that may occur in that disease. Such conditions as sinus arrhythmia, multiple extrasystoles, paroxysmal tachycardia and heart block of varying degrees are clinically familiar. The comparative rarity of conduction disturbances and their great interest alike on ætiological and prognostic grounds are the justification for this record of two cases that have come under personal observation during the last two years. A search has been made in the literature for previously published cases, and the results are presented briefly in this paper. In these, no attempt is made to differentiate "toxic goitre" and "hyperthyroidism" owing to the difficulty of correlating the divergent opinions of the writers quoted, and in many cases owing to absence of detail in reports.

The two cases reported here were treated under the charge of Dr Edwin Matthew in the Royal Infirmary, Edinburgh. We are indebted to him not only for access to the cases and permission to publish them, but also for much advice and help.

Case I.—M. T., female, aged 33, suffering from primary Graves' disease, was an in-patient during September 1928. Three weeks prior to admission she had had acute tonsillitis.

On admission pulse was 68, falling to 52 next day, being regular on both occasions. Electrocardiogram showed 2 : 1 heart block (see below). The following day auricular fibrillation developed; the pulse returned to regularity nine days later and remained so till discharge. Patient was four and a half months pregnant, and one week after discharge vaginal bleeding necessitated readmission, and abdominal hysterotomy under chloroform and ether anæsthesia. During this period in hospital auricular fibrillation was again present.

Twenty-seven months later readmission was necessary on account of cardiac failure, auricular fibrillation being clinically evident, and found to be associated with ventricular extrasystoles by electrocardiograph. Treatment produced a return to sinus rhythm, but upsetting domestic news, leading to discharge from hospital, resulted in a return of auricular fibrillation.

During these periods of observation heart block was found on the first occasion only.

Case II.—B. MacM., female, aged 18, was suffering from primary Graves' disease on admission to hospital on 1st October 1930. The pulse on admission was 120 per minute and showed sinus arrhythmia. Two months after admission she had an attack of acute tonsillitis, during which the pulse was more rapid but regular. Prior to tonsillectomy a septic tooth was removed under general anæsthesia (ethyl chloride) and one week later the tonsils and adenoids were removed also under ethyl chloride anæsthesia. Purulent post-nasal discharge was present for some days subsequently. Four days after the operation partial heart block was suspected clinically and confirmed by electrocardiogram (3 : 2). The further course of this heart block is shown by the series of electrocardiograms appended. After testing the reaction to various drugs (eserine sulphate and atropine sulphate hypodermically, and ergotamine tartrate intramuscularly), treatment was instituted with large doses of Lugol's iodine * and later ergotamine tartrate orally (see Charts 1 and 2).

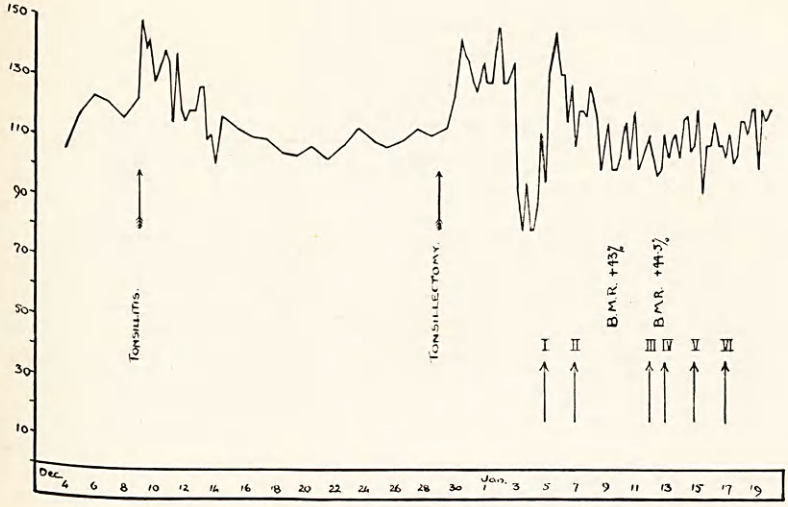
No improvement resulting from this treatment, operation was performed two months after disappearance of the heart block, $\frac{7}{8}$ of the gland being removed under gas and oxygen anæsthesia preceded by scopolamine and morphine. Electrocardiographic observation throughout induction and operation showed only a transient sinus slowing from 144 to 94 during induction. Post-operative course, followed by daily electrocardiograms, showed no return of the heart block. The operative treatment was carried out by Professor D. P. D. Wilkie and to him we have to acknowledge our indebtedness for permission to observe the patient before, during, and after the operation.

She has been examined on several occasions since discharge. The pulse rate has fallen to 80 per minute and sinus arrhythmia has been the only irregularity detected.

B.M.R. estimations before operation showed results of +43, +45 and +41 per cent. Repeated eight weeks after operation the result showed −3 per cent.

The pathologist reported on the removed tissue as "primary toxic goitre."

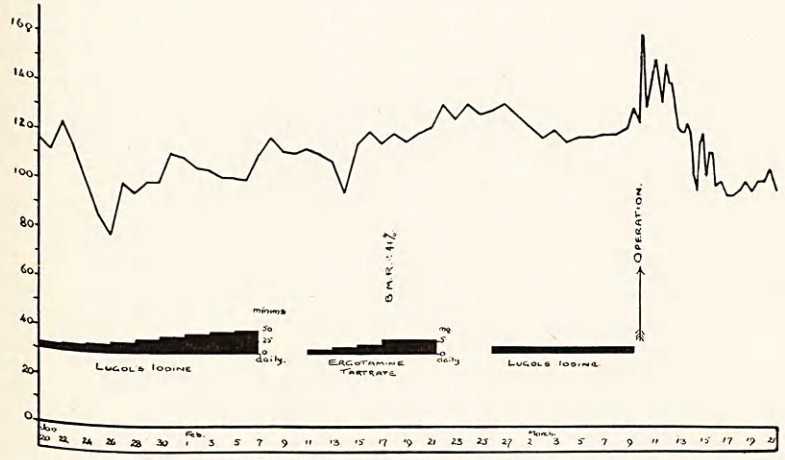
* Iodine 2, potassium iodide 3, water 40.



CASE 2. B. MacM. Chart of Pulse-Rate.

CHART 1.

I. Eserine sulphate gr. 1/150 H.I.; Atropine sulphate gr. 1/150. H.I. 30 minutes later.
II. Eserine sulphate gr. 1/100 H.I.; Atropine sulphate gr. 1/150. H.I. 30 minutes later.
III. Ergotamine tartrate 0·15 mgrm. I.M.
IV. Ergotamine tartrate 0·15 mgrm. I.M.
V. Ergotamine tartrate 0·19 mgrm. I.M.
VI. Ergotamine tartrate 0·25 mgrm. I.M.



CASE 2. B MacM Chart of Pulse-Rate. (continued.)

CHART 2.

CHARTS 1 and 2.—Case 2, pulse rate from 4th December 1930 to 21st March 1931. Showing fluctuations during tonsillitis, slowing due to heart block after tonsillectomy, response to various drugs, and response to operation.

Electrocardiograms.—Case I., Mrs M. T.

12.9.28.—Record three days after admission showed 2 : 1 heart block, alternate ventricular complexes being dropped. One extrasystole appears on the record: apart from it the ventricular rate is regular. The *P-R* interval varies between wide limits, with maximum of nearly 0·5 second (Fig. 1).

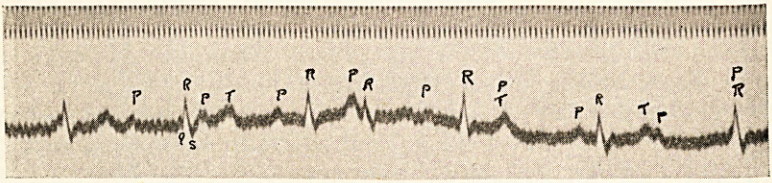


Fig. 1.—Electrocardiogram, Case 1, 12.ix.28: lead II. Time marker 28·57 per second. Record shows 2 : 1 heart block. The fourth ventricular complex is extrasystolic. (Reduced to 8/11.)

13.9.28.—The pulse was now wholly irregular, and electrocardiogram showed auricular fibrillation to be present. The initial deflections in this record are of much greater amplitude, and are less deformed than in the previous one: this type persists in all later records and may be taken as typical for this patient. The deformed initial complexes in the first record are apparently due to high resistance.

3.10.28.—Clinically auricular fibrillation was noted to disappear on 22.9.28, and the record on 3.10.28 shows normal rhythm with *P-R* interval prolonged to 0·24 second (Fig. 2).

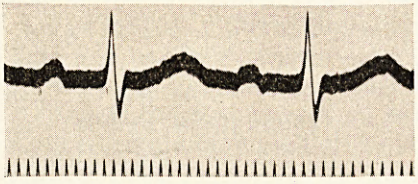


Fig. 2.—Electrocardiogram, Case 1, 3.x.28: lead II. Time marker 28·57 per second. Record shows delayed a.-v. conduction time, *P-R* being 0·24 second.

18.1.31.—Auricular fibrillation with ventricular extrasystoles.

9.2.31.—Normal rhythm following rest and Lugol's iodine: *P-R* interval 0·16 second.

17.2.31.—Auricular fibrillation re-established.

Electrocardiograms.—Case II., B. MacM.

3.1.31.—The first record, taken soon after the irregularity of the heart was noticed, shows partial heart block with *P-R* interva

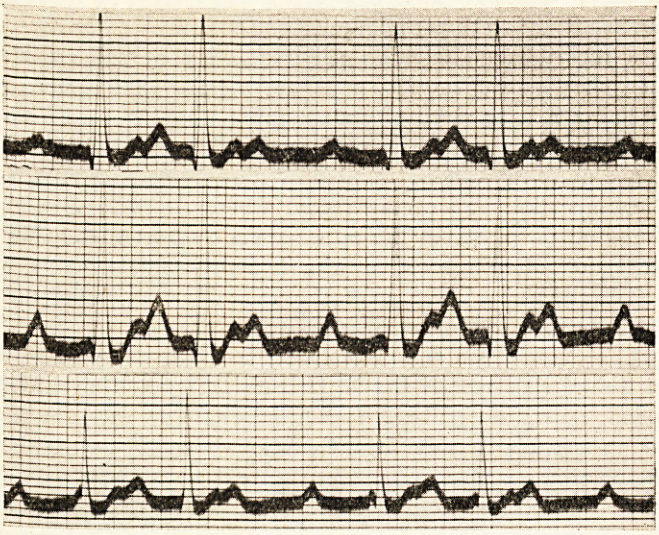


FIG. 3.—Electrocardiogram, Case 2, 3.i.31 : leads I, II and III. Time marker in this and succeeding records in fifths and twenty-fifths of a second. Record shows 3 : 2 heart block.

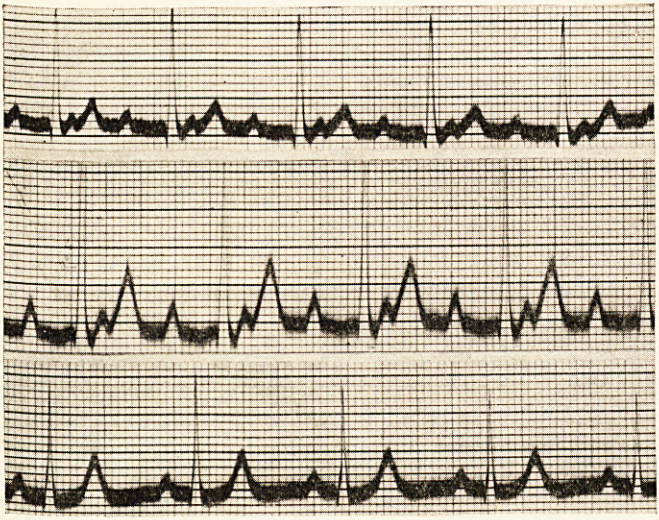


FIG. 4.—Electrocardiogram, Case 2, 4.i.31 : leads I, II and III. Record shows 2 : 1 heart block. In lead III alternate *P* waves are lost in *T* (see text).

prolonged to 0·24 to 0·3 second, and dropped beats (3 : 2 heart block): the auricular rate is 150 per minute (Fig. 3).

In a record taken later on the same day 2 : 1 heart block is present: the ventricular responses are regular, and clinically the patient had a regular pulse of 80 per minute, no signs of disordered cardiac action being evident on ordinary bedside examination. In this record one notes the varying relation of the *P* waves to the *QRS* and *T* deflections: in parts of the record where alternate *P* waves are superimposed on *T* waves the appearances suggest merely the high end deflection often associated with hyperthyroidism, along with a short *P-R* interval. Scrutiny of the record as a whole, however, affords a clue to the abnormal mechanism.

4.1.31.—A condition of 2 : 1 block persists, with complete regularity of the ventricular rate. Leads II and III, taken in immediate succession, illustrate again the loss of alternate *P* waves in the end deflection: lead III considered alone would probably be dismissed as showing no abnormality (Fig. 4).

5.1.31.—Coincident with a rise in the pulse rate to the 110 to 120 level, the dropped beats are found to have disappeared. A record on a fast plate shows the *P-R* interval to be 0·36 second (Fig. 5).

9.1.31.—From the form of the *T* wave and by analogy with previous records one may conclude that here again *P* and *T* are superimposed: the *P-R* interval is approximately 0·32 second. There are no dropped beats (Fig. 6).

17.1.31.—The *P-R* interval is now 0·16 to 0·18 second: the phasic alteration in the shape of ventricular complexes in lead III can be discounted—changes in the initial deflections in that lead accompanied the phases of respiration in this patient throughout the period of observation.

30.1.31.—The *P-R* interval has risen again to 0·2 second, at which level it remained for many weeks (Fig. 7).

Caroto-vagal Pressure.—Right-sided stimulation produced marked auricular slowing, the *P-P* interval rising from an initial value of 0·48 to 0·76 second. Conspicuous ventricular slowing also occurred, a transient condition of 2 : 1 heart block being established. As the auricular rate rose on release of the pressure, the block increased to 3 : 1, fell back to 2 : 1 and then returned to its initial stage—long *P-R* without dropped beats.

Left-sided stimulation had conspicuously little effect upon the auricles, *P-P* rising from 0·44 to a maximum of 0·48 second: a transient heart block reaching 3 : 1 in one instance was, however, again established.

Respiratory Effects.—Inspiration shortened the *P-R* interval by 0·04 second without any ventricular arrhythmia being present.

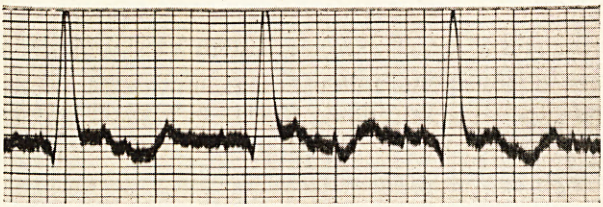


FIG. 5.—Electrocardiogram, Case 2, 5.i.31 : lead II. Record shows delayed a.-v. conduction time, *P-R* being 0·36 second. *P* falls in each case between the *QRS* and *T* of the preceding complex.

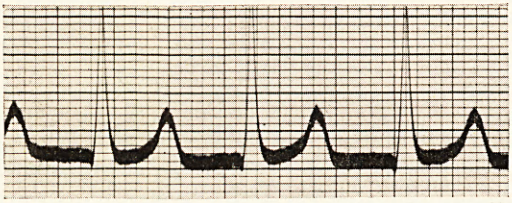


FIG. 6.—Electrocardiogram, Case 2, 9.i.31 : lead II. Record shows superposition of *P* and *T*, with *P-R* of 0·32 second.

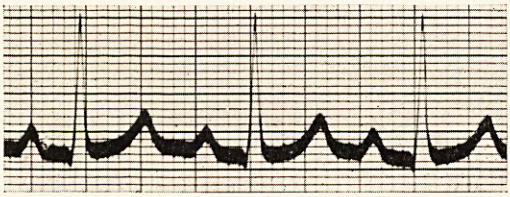


FIG. 7.—Electrocardiogram, Case 2, 30.i.31 : lead II. *P-R* now measures 0·2 second.

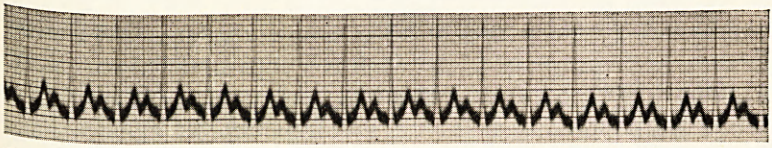


FIG. 8.—Electrocardiogram, Case 2, 10.iii.31 : lead II. The record was taken at the beginning of induction of anæsthesia with gas and oxygen immediately before operation. Sinus rhythm at 144/minute, with *P-R* of 0·16 second. (Reduced to 8/11.)

Effects of Drugs.—(Observations on CASE II only.)

Eserine and *atropine* were alike without significant effect on pulse rate or conduction time.

Lugol's Iodine:—Beginning with min. v., t.i.d., Lugol's Iodine was given orally in increasing doses for nineteen days, by which time a daily dose of min. xlviii. had been reached. Small

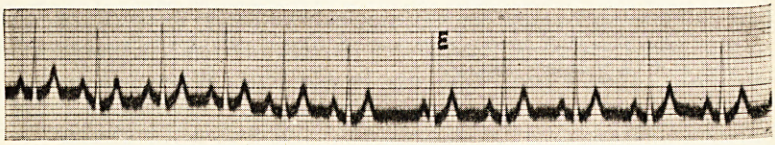


FIG. 9.—Electrocardiogram, Case 2, 10.iii.31 : lead II. Record a few minutes later. The auricular rate has slowed to 94/minute, with no change in *P-R* interval. At *E* there is escape of the ventricle. (Reduced to 8/11.)

doses had as usual a beneficial effect on the pulse rate, which was not maintained under larger doses. A pre-operative course with min. xv. daily for thirteen days produced, as expected, little effect on the pulse rate, but at operation the gland was found to be satisfactorily iodised.

Ergotamine tartrate was used on several occasions by intramuscular injection, the action being followed by electrocardio-

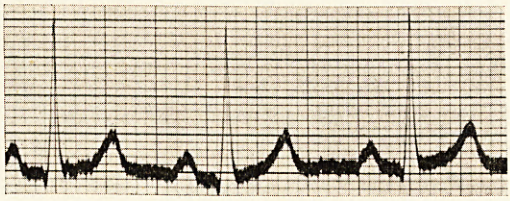


FIG. 10.—Electrocardiogram, Case 2, 17.iii.31 : lead II. (One week after operation). *P-R* equals 0·16 second.

graph, and by pulse and blood pressure readings (see charts). In view of its property of paralysing sympathetic fibres (Dale,[6] Rothlin [30, 32]), and of the published reports of lengthened conduction time produced in the normal mammal (Andrus and Martin [3]), and in hyperthyroidism cases in man (Merke and Eisner [25]) by its administration, it was used in this case in an attempt to modify the conduction time, and the height of the electrocardiographic deflections. Though moderate slowing of the whole heart was elicited, along with changes in blood

pressure, etc., no effects on conduction, or on the *P*, *R* and *T* waves, were demonstrable (Chart 3 and Figs. 11, 12 and 13). The action was transient, and clinically associated with symptoms of intolerance (nausea, and præcordial constriction) after doses so small as 0·125 mg. intramuscularly, though larger doses later were without untoward effects. The drug was later given orally over a period of days, again with symptoms of intolerance, but with no results indicating that it was of therapeutic value.

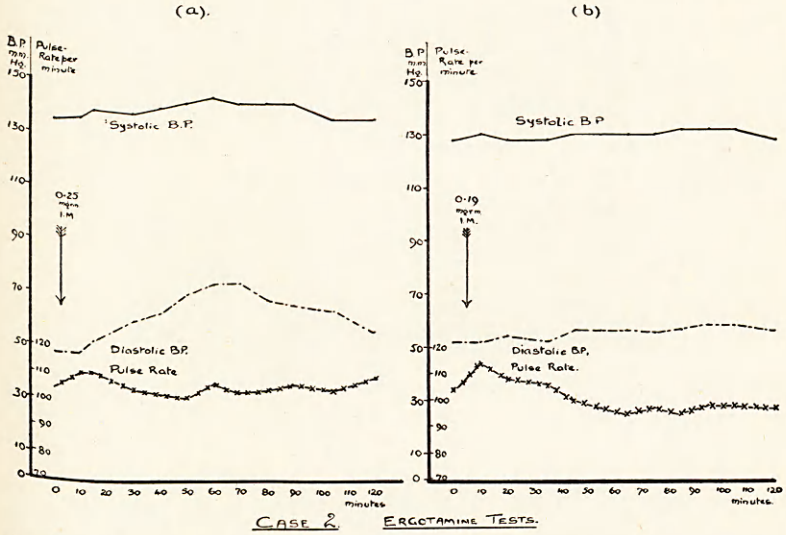


CHART 3. (a) and (b).—Case 2, ergotamine experiments. Charts showing changes in pulse rate, and in systolic and diastolic blood pressures after intramuscular injections of ergotamine tartrate in doses of (a) 0·25 mg., and (b) 0·19 mg. Note in (a) marked rise in diastolic pressure, and in (b) slowing of pulse rate. Both effects are transient.

Paralysis of sympathetic fibres can only be elicited in animals after doses that are much larger than can safely be given to man. The therapeutic use of the drug in hyperthyroidism (Adlersberg and Porges,[1] Jagic,[19] Merke,[23, 24] Merke and Eisner,[25] Noyons and Bouckaert,[27] Rothlin,[31] Stähelin,[35] Youmans, Trimble and Frank[42]) resting on this basis, is therefore of questionable utility, even if one accepts the premise that the cardiac effects of the disease are due to sympathetic overaction (Enderlen and Bohnenkamp[11]). The dangers of peripheral gangrene (Merke[24]) and of acute circulatory disturbances (Jagic[19]) further oppose its general use.

Incidence of Heart Block in Previously Published Series.—Probably the earliest reference to this condition lies in a publication in 1880 by Merklen,[26] who gives a clinical description of a case of toxic goitre where apparent Adams-Stokes' seizures occurred. A second reference to the occurrence

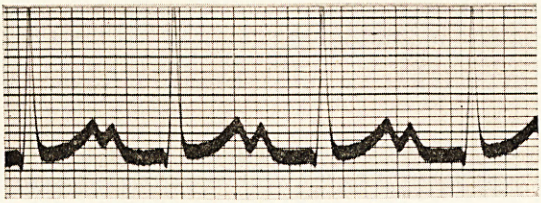


FIG. 11.

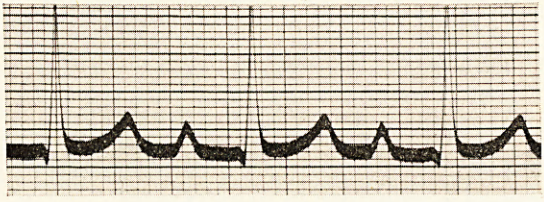


FIG. 12.

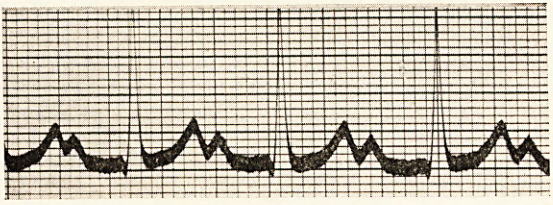


FIG. 13.

FIGS. 11, 12 and 13.—Electrocardiograms, Case 2, 15.i.31: lead II. To show the effect of ergotamine tartrate, given intramuscularly (0.19 mg.) at 11.45 a.m. First record at 12 noon, second at 1.35 p.m., third at 4.55 p.m. Transient slowing of whole heart without effect on conduction.

of complete heart block in a goitrous case occurs in the paper of Reilingh[29] in 1915. Since 1918 various papers have appeared giving details of the cardiac condition of large series of patients suffering from toxic goitre. The frequency of heart block in these is summarised in the accompanying table along with our own figures. Cases showing heart block are classified

in order of severity, as showing simple prolongation of *P-R* interval, dropped beats, or complete heart block.

Author.	No. of Cases examined with Electro-cardiograph.	Cases of Heart Block.			Remarks.
		PR+	D.B.	C.H.B.	
Krumbhaar[21] (1918) . .	51	2	...	...	...
White and Aub[39] (1918) .	47	...	...	1*	? not all "toxic goitre."
Kerr and Hansel[20] (1923) .	25	3	...	...	...
Willius and Boothby[41] (1923)	377	1	...	...	One S-A block.
Dameshek[7] (1924) . . .	141	2	...	2	(See text).
Smith and Colvin[34] (1926) .	100	0	...	...	All B.M.R.'s over + 30%
Andrus[2] (1929) . . .	86	1	...	...	Average B.M.R. + 45%
Goodall and Rogers[14] (1927) .	787	242	...	...	...
Parkinson and Cookson[28] (1931)	130	0	...	...	...
Writers' Series† . . .	100	2	3	...	...

* Case one of myxœdema reported in detail by Aub and Stern.
† Figures from Clinical Laboratory, Royal Infirmary, Edinburgh.

In Dameshek's series the four cases with conduction defect occurred in young people (ages 36, 31, 29 and 26 years) with high basal metabolic rates (+ 60 per cent. in the three cases where it was estimated), points on which that author lays some stress.

Various authors have reported single cases of heart block occurring in cases of goitre. The cases of Strauss[36] and of Simon[33] are examples of heart block occurring as an incidental in cases of non-toxic goitre. In Strauss' case the patient had had heart block and auricular flutter for over twenty years, along with an adenoma of the thyroid, and the block persisted after operative removal of the tumour. In the other, the block developed after operative removal of a very large goitre, and was attributed to vagal damage and hyperexcitability. Such cases may be dismissed as not material to the subject.

The case of Eason[9] presents features very similar to those of our present cases. In 1930 he described a case of partial heart block with dropped beats and long *P-R* interval occurring in a woman of 25, the subject of hyperthyroidism Some weeks before admission to hospital she had had tonsillectomy performed without adequate pre-operative treatment. There was marked local septic infection in the throat, the soft palate having perforated on account of sloughing, and

septicæmia was present. The onset of block was heralded by a syncopal attack. In a previous publication[8] the same author states that delayed conductivity is by no means uncommon in goitre cases.

A number of writers on the heart in toxic goitre either make no mention of heart block (Hurxthal,[18] Brodie,[5] Franke,[13] White[38]) or dismiss it as rare or exceptional (Foster,[12] Jagic[19]). Conversely, in analyses of series of cases showing heart block, one does not find mention of toxic goitre among the ætiological agents (White and Viko,[40] Lewis,[22] Wenckebach and Winterberg[37]).

The figures of Goodall and Rogers[14] stand out in sharp contrast to others in the table, and are contrary to this general verdict as to the rarity of the condition, a discrepancy that is difficult of explanation.

Our personal experience is more in accord with the general finding; though the incidence in our series is double the general average, it falls far short of Goodall and Rogers' high figure.

Association with Throat Infections.—It is noteworthy that in both of the cases here reported the development of heart block followed upon septic throat infection. In one case the onset of heart block occurred three weeks after a "sore throat"; in the other, six days after tonsillectomy undertaken in consequence of a recent tonsillitis. In the case of Eason,[9] the disorder was also noted to occur some weeks after a tonsillectomy. The question arises as to how far the tonsillitis and the hyperthyroidism were respectively responsible for the cardiac condition.

Wenckebach and Winterberg[37] state that severe sore throats, especially of streptococcal origin, are frequent causes of marked functional disturbances in the conduction system, and add that the same holds for septic conditions in general. Yet, considering the frequency of sore throat, the incidence of heart block in that condition must be low.

There is a certain amount of evidence that hyperthyroidism can cause myocardial lesions. Hashimoto[17] produced such lesions in rats by thyroid feeding. Goodall and Rogers[15] in reporting a clinical case showing toxic myocardial changes post-mortem state that "sustained thyrotoxicosis ultimately results in definite myocardial degeneration." On the other hand Goodpasture[16] in thyroid feeding experiments in rabbits

found no significant myocardial changes unless the animals had also been subjected to light chloroform anæsthesia. Commenting on this, East and Bain[10] suggest that myocarditis only occurs when some other agent acts along with thyroxin. They suggest that any general anæsthetic may be dangerous in hyperthyroidism for this reason.

In each of the cases here reported such a double intoxication was present: those of the throat condition and of the hyperthyroidism. On recovery from the throat infection the block in each case disappeared. In Case I., the auricular fibrillation following upon the block renders conclusion difficult, but the high ventricular rate after an abdominal operation under general anæsthesia precludes recurrence of damage to the conduction system. In Case II., the block did not recur during the ten weeks before operation, though the cardiac condition otherwise remained of unchanged severity: nor did it recur during the anæsthesia or the post-operative period, in both of which the case was under close electrocardiographic observation. It would appear therefore that the thyroid intoxication rendered the myocardium susceptible to the noxious influence of the throat condition, and that the latter was the precipitating cause of the block. The rôle of the anæsthetic would hardly appear to be so important as suggested by East and Bain.[10]

Summary.—1. Two cases of heart block complicating toxic goitre are reported, with an account of their subsequent course as followed by the electrocardiograph.

2. The effect of various drugs and anæsthetics on the condition is recorded.

3. An association with recent throat infection was noted in each case: this relation is discussed.

4. The comparative rarity of heart block as a feature of such goitre cases is illustrated by a series of 1744 cases drawn from the literature.

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