THE INFLUENCE OF ATROPIN UPON COMPLETE HEART BLOCK, TRANSIENT AND INTERMITTENT

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THE influence of atropin upon people with complete heart block varies from case to case. Sometimes normal sinus rhythm follows the administration of the drug, at other times there is merely a variable degree of auricular and ventricular acceleration. The deciding factors in the response are the process or processes governing the arrhythmia and the dose and mode of administering the drug. Where complete heart block is transient, acute infections such as rheumatic, diphtheria, influenza, gonococcal and septic endocarditis, pneumonia and scarlet fever are primarily responsible for the disorder (Cowan and Ritchie, 1935). Of these, diphtheria is the principal offender (Campbell and Suzman, 1934), while coronary disease rarely gives rise to the disorder. Atropin, given during transitory arrhythmia, has succeeded in producing normal sinus rhythm in a patient with rheumatic fever (Rosenson, 1924) and in another with coronary thrombosis (Wedd, 1937), but Steuer (1936) failed to confirm the results in an individual suffering from thyrotoxicosis.

On turning to the group of cases with intermittent complete heart block, it should be understood that where impaired conduction precedes the development of this arrhythmia it will be classified as type I, but should delayed conduction be absent between the paroxysms of complete block it will be termed type II. Type I is usually due to a chronic obliterative process of the coronary arteries, and the commonest precipitating factor is probably digitalis therapy (Ellis, 1932). As is well known, digitalis may have this effect in people who have a normal or prolonged P-R interval. For example, complete block occurred in a normal individual after a toxic dose of digitalis had been given by McGuire and Richards (1936). Such a change arises more readily where the heart is diseased, as has been demonstrated in 16 cases by Robinson (1922), Cohn (1913), Hewlett (1910), Christian (1915), Wedd (1919), Luten (1925), Stecher, (1929) and Wilkinson (1942). Three more examples have been recorded in patients suffering from chronic myocarditis or

coronary disease, and in these the reaction to atropin has been studied.

CASE 1 showed complete heart block precipitated by digitalis therapy, and subsequently abolished with atropin sulphate. The patient's name was Miss A. P. She was 69 years of age and had a history of coronary thrombosis three months prior to admission to hospital. There was probably a recurrence of coronary occlusion six weeks after the onset of symptoms, and again on the day she was admitted to hospital (3.2.41). When she arrived in the ward she was almost moribund, with acute left ventricular failure; she was orthopnœic, cyanosed and froth poured from her mouth on account of the pulmonary œdema. After three months on treatment she was sitting comfortably in bed, taking her food well, and sleeping soundly at night. Signs of heart failure had vanished, and electrocardiographically she exhibited partial heart block (P-R interval 0.44 second), and dropped beats. The lady was then given tincture of digitalis m. xxx t.i.d., which produced coupled rhythm three days later. The following day (3.5.41) she became nauseated, and her electrocardiogram was taken before, during and after intravenous injection of atropin sulphate gr. $\frac{1}{30}$. Complete heart block present at first was replaced by normal sinus rhythm seventy seconds after the atropin injection (electrocardiogram I and II, lead 2).

CASE 2 exhibited complete heart block occurring with digitalis therapy and sometimes terminated with atropin. The observations were made on Mr P. H., aged 66, who was admitted to hospital on 7.11.40 with a history of minor Stokes-Adams seizures over a period of four months. They took the form of faintness and a sensation of pressure under the left lower ribs anteriorly, either while walking uphill, or, less frequently, while resting. The attacks only lasted a few seconds. On examination, the patient was well preserved for his years, intelligent, alert and co-operative. Clinically there was no evidence of disease, but electrocardiographically partial heart block and common type bundle branch block were recorded (12.11.40). Eleven days after admission (18.11.40) he experienced several Stokes-Adams seizures after taking tincture digitalis half a drachm three times a day for five days. Complete heart block had developed with an auricular rate of 85 and a ventricular rate of 30. In addition the bundle branch block was accentuated, the base of the QRS complex measuring 0.18 instead of 0.12 second.

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Further digitalis therapy was therefore abandoned. Intravenous atropin sulphate gr. $\frac{1}{30}$ did not alter the rhythm, but there was an acceleration of the auricular and ventricular contractions. Four days later (22.11.40), normal sinus rhythm returned spontaneously, and with it the time interval for the QRS complex reverted to its original length, 0.12 second. Ten days after this (2.12.40) the patient was noted to have complete heart block (electrocardiogram III). A dose of atropin similar to that which had been given previously was injected, with the result that a 3:1 auriculo-ventricular response was recorded within fifty-six seconds and normal sinus rhythm without dropped beats after another two minutes had passed (electrocardiogram IV, lead 2). Thirty-six days after admission (13.12.40) nausea occurred after four drachms of digitalis had been taken during the preceding sixty hours. Both complete heart block and an increase in the bundle branch block returned, and in addition coupled rhythm developed due to the presence of ventricular extra systoles. The usual dose of atropin succeeded in abolishing the extra systoles but the conduction defect remained. The following day, however, the injection of atropin was repeated and normal sinus rhythm with bundle branch block returned (25.12.40).

CASE 3.—Atropin failed to abolish transient complete heart block produced by digitalis therapy. This was observed in a man, J. W., aged 59, admitted to hospital 27.4.40. Five months prior to admission he first noticed that his feet and ankles became swollen after his day's work. A month later the swelling became more marked, and the amount of work he was able to do was limited by breathlessness. About three months before admission he was compelled to give up work owing to marked breathlessness and extensive œdema of his legs. On being admitted to hospital he still had slight œdema of legs and over the sacrum, fluid was present at the base of the right lung and his liver was enlarged. His pulse rate was 120 and blood pressure 120/90. There was heart failure with gross cardiac enlargement and mitral incompetence. The electrocardiogram, four days after his admission, showed auricular fibrillation, left axis deviation and ventricular extra systoles. During the following forty-two days he consumed $36\frac{1}{2}$ drachms of tincture digitalis. With this treatment he was nauseated and very peculiar mentally. His electrocardiogram No. V (11.6.40) showed complete heart block with an auricular rate of 130 and a ventricular rate of 77. These

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rates increased to 140 and 83 respectively after atropin sulphate gr. $\frac{1}{30}$ had been given intravenously. Two days later, after

ELECTROCARDIOGRAM.

another drachm of digitalis had been given, the atropin test was repeated. This time there was no acceleration of either auricular

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or ventricular contractions, their rates being 130 and 66 respectively, and the complete block persisted. Digitalis therapy was then terminated, and eleven days later the patient had normal sinus rhythm.

When atropin is administered to cases of intermittent complete heart block (type I) variable reactions are obtained. For example, extract belladonna gr. $\frac{1}{4}$ taken orally five times a day failed to prevent recurrent attacks of complete heart block in a patient suffering from coronary sclerosis (Dubbs, 1938). In another case, arising from digitalis poisoning, atropin was unsuccessful in producing normal sinus rhythm (McGuire, 1936). In contrast to this, atropin gr. $\frac{1}{16}$ and gr. $\frac{1}{80}$ given hypodermically to an individual in congestive heart failure abolish the complete heart block which had been precipitated by digitalis therapy (Cohn, 1913). Furthermore, Wedd (1919) managed to convert complete block to normal sinus rhythm in two people intoxicated with digitalis by injecting atropin gr. $\frac{1}{32}$. Case 1 of the present series substantiated Wedd's observation while case 3 supports McGuire's finding. An intermediate response exemplified in case 2 demonstrates how atropin gr. $\frac{1}{30}$ twice failed to abolish the disorder, but after an interval of time during which digitalis had been omitted the same dose of atropin twice succeeded in producing normal sinus rhythm. Therefore, the reaction is partially dependent upon the degree of digitalisation.

Type II, intermittent heart block, may be defined as one which occurs at intervals in an individual who normally exhibits a normal conduction time between the attacks, but it includes cases which temporarily develop defective conduction following the period of complete block. This latter feature was present in the cases reported by Wilson (1918), Carter (1931) and Sachs (1933). Fourteen cases fulfilling the definition have been tabulated to show their ætiology and reaction to atropin. From these it can be concluded that degeneration of the bundle of His is the dominant factor in the causation of the arrhythmia, and that either oral or hypodermic atropin will sometimes prevent the disorder. Intravenous atropin in cases 4 and 5 terminated the block, as will be seen from the following records:—

CASE 4 illustrates how the rare type of complete heart block can be abolished with atropin sulphate. Mrs E. F., aged 55, admitted to hospital 18.4.41, had experienced "fainting attacks" for four years. With the first attack she was unconscious for ten

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minutes. Four months later she had a series of seven faints during one week while she was under observation in hospital, and she proved to be suffering from intermittent heart block associated with Stokes-Adams seizures. Three years later she was again admitted to hospital for a recurrence of her fits. Physically, she was an obese, middle-aged woman, rather excitable and anxious about herself. She had no abnormal physical signs apart from a dermatitis on her chest for which she was receiving

TABLE

Author.	Ætiology.	Atropin.	Reaction.
Earnshaw	Arteriosclerosis	gr. 1/60	Block persisted
Simon and Robinson .	Arteriosclerosis	gr. 1/50	Block unaffected
Carter and Dieuaide .	Arteriosclerosis	gr. 1/32	Block persisted
Wolferth and McMillan	Lesion of A-V bundle	gr. 1/20	Block persisted
Carter and McEachern	Arteriosclerosis	gr. 1/240 Hypo.	Block persisted
Sachs and Traynor .	Rheumatic	gr. 1/30 Hypo.	Attacks persisted
Corneau	Arteriosclerosis	gr. 1/60 t.i.d.	Attacks persisted
McIntosh and Falconer	Arteriosclerosis	gr. 1/100 orally t.i.d.	Prevented block
Gayer and Pardee .	Rheumatic	gr. 1/100 orally q.i.d.	Prevented attacks
Cheer and T'ang .	Rheumatic	gr. 1/240 Hypo. daily	Prevented attacks
Weiss and Ferris— Case 1	Esophageal diverticulum	gr. 1/24 Hypo.	Prevented attacks
Case 3	Neuro-oesophageal reflex	gr. 1/24 Hypo.	Prevented attacks
This series Case 4 .	Obscure	gr. 1/30 I.V.	Terminated three attacks
„ „ Case 5 .	„	gr. 1/30 I.V.	Produced sinus rhythm for 28 seconds

treatment. Her blood pressure was 140/80. Her heart radiologically was enlarged and her aorta tortuous. She had no valvular lesion.

Electrocardiogram VI (18.4.41) showed that complete heart block was present with an auricular rate of approximately 85 and a ventricular rate of 17 beats per minute. In this record the thick vertical lines indicate the beginning and end of the injection of intravenous atropin gr. $\frac{1}{30}$. Seventy-two seconds later 3:1 auriculo-ventricular response was recorded with an auricular rate of 116 (electrocardiogram VII), but when the auricular rate fell to 108 the response became 2:1. This was again demonstrated 18 days and 35 days later (6.5.41 and 23.5.41).

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The influence of exercise was as remarkable, for on three occasions (2.5.41, 9.5.41 and 13.5.41) complete heart block replaced 2:1 block when the auricles were beating between 120 and 150 times per minute. The amount of work required to precipitate this transformation was 6048 to 6426 ft.-lb. in two minutes. The change, however, was very transitory, for high grade partial block was recorded after approximately two minutes' rest. During one of these tests (9.5.41), when 6048 ft.-lb. work was performed, 4:1 auriculo-ventricular response appeared as the heart recovered from complete heart block. Yet another interesting observation was made following the exercise test on 23.5.41 when the transition from complete heart block to sinus rhythm began by every idioventricular beat alternating with a driven sino-auricular beat (electrocardiogram VIII).

CASE 5 demonstrates how atropin temporarily abolished complete heart block in a woman, Mrs J. MacP., aged 73. She was admitted to hospital on 16.2.40 because she had vomited a cupful of blood. In the past she had been troubled with abdominal pain coming on half an hour after meals and relieved with alkalies.

On examination she was conscious and had a good colour. She had no signs of heart failure. The blood pressure was 140/60 and the pulse rate 60. Her heart was enlarged, the apex beat being in the sixth intercostal space in the mid-axillary line. On auscultation the heart sounds were of poor quality. In the mitral area the first sound was followed by a soft systolic murmur. Examination of the chest revealed emphysema, but the abdomen was apparently normal.

On the night of admission the patient had another hæmatemesis. The following day she had Cheyne-Stokes breathing and was drowsy and speechless. Her electrocardiogram showed a bradycardia with A-V dissociation. During the following three days her condition did not improve and she died on the fourth day from severe hæmorrhage from a gastric ulcer and terminal hypostatic bronchopneumonia. This was confirmed later at autopsy.

A few hours before death she had complete heart block with changing idioventricular rhythm which was interrupted by isolated sino-auricular beats after 1-20 cardiac contractions. The ventricular rate was initially 66-69 and the auricular rate twice as fast. Atropin gr. $\frac{1}{30}$ was injected intravenously and this was followed 82 seconds later by normal sinus rhythm.

The transition from idioventricular rhythm to normal sinus rhythm is shown in electrocardiogram XI, where it will be noted that there was a 2 : 1 heart block, the P-R interval being 0.16 seconds. The normal rhythm lasted 26 seconds when it was replaced by complete heart block with variable QRS complexes as had been observed prior to the administration of atropin. The rate was still 69, but during the period when normal sinus rhythm was recorded the rate temporarily rose to 71. Further observations could not be made, as she died within a few hours of the test.

Conclusion and Summary.—In four cases of transient or intermittent complete heart block atropin given in toxic doses produced normal sinus rhythm, but it failed to do so in one case of complete heart block. In this particular case normal sinus rhythm appeared spontaneously after digitalis therapy had ceased for eleven days. On correlating these results with those recorded in the literature, it can be stated that type I or type II complete heart block may or may not be abolished by atropin. The facility with which the drug brings about the transformation does not depend so much on the ætiology of the disorder as on the extent and severity of the lesion. Tachycardia or digitalisation may also modify a reaction, the former accentuating defective conduction in type II heart block, while digitalis therapy sometimes impairs the conduction of the bundle of His to such an extent that atropin fails to abolish the complete heart block.

The manner in which complete heart block passes to sinus rhythm or vice versa has been studied in case 4 with the rare type of intermittent block, and it may be concluded that a 3 : 1 auriculo-ventricular response usually develops either prior to or following complete block. Rarely a 4 : 1 response was recorded when the auricular rate rose to 138 beats per minute. In one instance the first step in the passage from complete heart block to sinus rhythm was effected by every idioventricular beat alternating with a driven sino-auricular beat, so that an inconspicuous type of coupling of ventricular complexes was observed. In case 5 the transition from complete block was somewhat similar in that the frequency of auricular impulses conducted to the ventricles increased after atropin administration but in a non-rhythmical fashion.

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