event 40 minutes or even longer after epidural injection of what might have seemed a not too excessive dose in a patient of normal biological age.

Summary

Injection of local anaesthetic solutions into the spinal extradural space results in a segmental type of analgesia. In normal subjects the number of analgesic dermatomes can be predicted with an accuracy of 15 to 30% in terms of age and the concentration and volume of local anaesthetic used. The amount of local anaesthetic required to block a given area declines steadily after the second decade, in a manner reminiscent of some other curves relating biological phenomena to age.

Fifty-three patients with occlusive vascular disease reacted abnormally to epidural analgesia. They behaved as if they were 25 to 50 years older than their chronological age, or as if the injected solution had been twice the concentration actually used. In these patients segmental analgesia spread one and a half to three times further than in normal subjects of the same age. This tendency to increased spread can be hazardous if the anaesthetist is not aware of the necessity for reduced dosage in arteriosclerotic patients.

The time taken for epidural analgesia to reach its farthest limits varies quite widely in normal subjects, and does not appear to be dependent on age. This time interval is prolonged in arteriosclerotic patients.

The significance of these findings is discussed in relation to the effects of ageing processes, and to the site of action of epidural analgesia.

I am grateful to my colleagues in the Department of Anaesthesia, Royal Victoria Hospital, Montreal, for their help in carrying out this study. Supplies of lignocaine were provided through the kindness of Astra Pharmaceuticals Inc., Worcester, Mass., U.S.A.

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A SYNDROME DUE TO TRANSIENT OR CHANGING HEART-BLOCK

BY

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It is well recognized that angina pectoris can occur with the paroxysmal tachycardias. Pain can also be a direct result of heart-block, the pain and the block starting and ending at the same time.

Four cases of transient or changing heart-block are reported. Two of the patients had normal cardiograms at rest and had severe pain only when exertion was associated with a 2 : 1 heart-block. The pain was described as bursting, relieved by a varying period of rest but not by trinitroglycerin, and radiating to the neck and down the arms. The pain was associated with the sudden onset of severe dyspnoea, palpitations, a feeling of marked faintness, weakness of the limbs, and alarm. In the other two cases symptoms were associated with a change from 2 : 1 to a complete heart-block.

Froment *et al.* (1959) report three cases of anginal pain associated with heart-block but without evidence of coronary artery disease. They believe that myocardial anoxia results from the decrease in coronary blood flow with the abrupt slowing of the heart rate. This is discussed later.

Exercise has an important effect on the ventricular rate in both complete and partial heart-block. It was once thought that the bradycardia of complete heart-block was quite unaltered during exercise (Vaquez, 1924), but Gilchrist (1934) showed that the idioventricular centre and the sino-auricular node react qualitatively in the same way to different stimuli. Partial atrioventricular block is also affected by exercise, and in fact two types can be distinguished by their response to exercise. In the benign type 1 partial heart-block of the Wenckebach variety, with progressive lengthening of the P–R interval, exercise eliminates the block ; whereas in the more serious type 2 partial atrioventricular block, with the fixed P–R interval, exercise may change a 2 : 1 to a 3 : 1 or to a complete heart-block (see Cases 3 and 4). Exercise may also bring to light a type 2 block when under resting conditions a cardiogram is normal (see Cases 1 and 2).

Thomson (1934) found only one case of type 2 partial block among 5,000 patients electrocardiographed. By exercise tests and other methods of auricular acceleration, such as the use of atropine and amyl nitrite, Gilchrist (1958) has shown that type 2 partial block is not rare. He found 24 examples of type 2 atrioventricular block among the 140 patients with high-grade heart-block that he has studied clinically. In that authoritative article, only one passing reference to angina is made : " fatigue, exertional dyspnoea, mild to moderate in degree, and attacks of effort angina may prove more of a handicap than the liability to syncope."

In the cases reported here a characteristic symptom-complex appears to result from the onset of heart-block or change in the degree of block which is usually provoked by exercise. If exercise tests were done more commonly in patients with symptoms described here, and in whom a resting cardiogram showed no heart-block, more cases of type 2 partial block and this clinical syndrome might well be recognized.

Case 1

A man aged 55 was referred in September, 1961, to the medical out-patient department with a 10-months history of dyspnoea and chest pain on exertion with ankle oedema. He had been treated by his doctor with digitalis and chlorothiazide for heart failure and given trinitroglycerin for the chest pain. He lost consciousness on one occasion, and on recovery had a retrosternal chest pain. The practitioner diagnosed a cardiac infarction.

When he was first seen in the out-patient department the pulse was 88 and regular and the blood-pressure 135/95. Clinical examination was essentially negative. A cardiogram showed splintering of the QRS complex in lead III and a flat T wave which became normal on inspiration. The tracing was otherwise normal. A chest *x*-ray film showed no abnormality and the blood cholesterol was 273 mg./100 ml.

The patient remained well for three months, but in January, 1962, symptoms recurred, and in February he was referred back to the out-patient department. He complained of a peculiar bursting feeling in the chest, usually brought on by exertion but also occurring spontaneously at rest without emotional stimuli and occasionally persisting for hours. When the pain was present on exertion, relief would come on resting after a variable period, but relief was not afforded by trinitroglycerin. Dyspnoea and a feeling of faintness accompanied the pain when it occurred on exertion.

A cardiogram done when the pain was present showed a 2:1 block. The tracing was otherwise identical with that done four months earlier (see Fig. 1 a). The patient was being treated at this time with digitalis folia 1 gr. (65 mg.) b.d., but this was discontinued.

In March his symptoms had greatly improved. A cardiogram was now done with an exercise test. Exercise produced marked depression of the R–T segment in V_4 with only very slight retrosternal discomfort. On this occasion no 2:1 block occurred (see Fig. 1 b). Thus exercise produced changes of myocardial ischaemia with virtually no pain, whereas a 2:1 block without ischaemic changes produced severe symptoms.

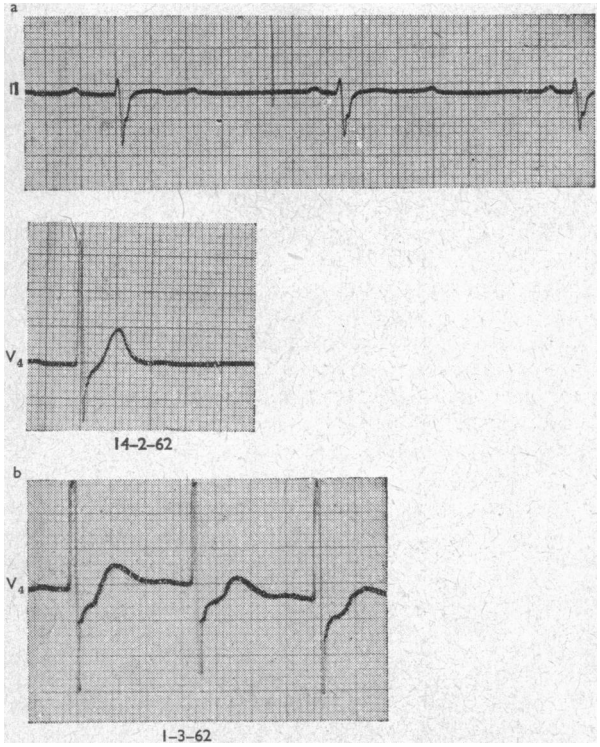

FIG. 1.—Case 1. Cardiogram showing (*a*) tracing when pain was present showing 2:1 block; and (*b*) tracing when pain was very slight with marked ischaemic changes on exertion but no block.

Case 2

A married woman born in 1900 gave a history of headaches since childhood. The headaches became worse in 1943, when hypertension was discovered and treated by periodical venesection. In 1949 her blood-pressure was 190/120 and she had the usual investigations for hypertension. The cardiogram was normal at that time. She was treated by lumbar sympathectomy, the second side being done in March, 1950. The headaches recurred about three months after the operation.

In August, 1953, she returned with new symptoms, and since their onset she has had less trouble with headaches. She complained of attacks of central chest pain. The pain often woke her and also occurred during the day on exertion. She complained of palpitations in association with the pain and throbbing in the bridge of the nose. Further cardiograms showed no abnormality. It was thought that her symptoms were due to gross sensory hysteria with a cardiac neurosis.

From 1953 to 1961 the severity of her different symptoms varied from time to time. On October 10, 1961, it was noted that the pain always occurred on exertion but was not relieved by trinitroglycerin. She was then exercised and the pulse found to be 64 and regular after exertion, but the blood-pressure fell to 120/60 from a resting value of 190/115. She felt faint but had no pain on this occasion. The faintness was attributed to post-exertional hypotension, an effect seen in some patients with hypertension (Fowler and Guz, 1954).

After walking up and down 30 steps she had chest pain, palpitations, and faintness. The pulse became irregular and a cardiogram showed that she had a varying 1:1, 2:1 heart-block. A 2:1 heart-block occurred again within three minutes of exercise consisting alternately of touching the toes and lying back. The heart-block ceased in three minutes at the same time as the symptoms subsided, to recur when the patient was dressing (Fig. 2 a and b).

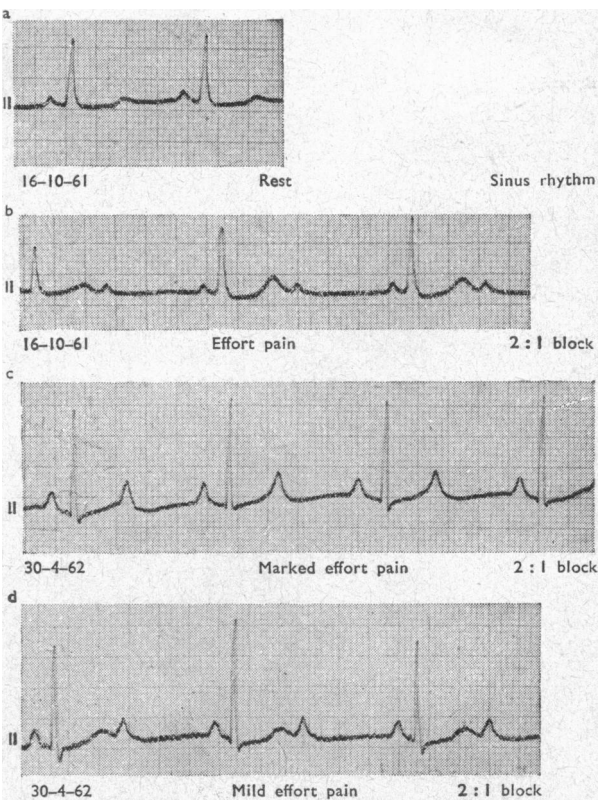

FIG. 2.—Case 2. Cardiogram showing 2:1 block occurring with effort pain. (*c*) Alternate P waves buried in the T waves. (*d*) Separation, with milder effort.

On April 30, 1962, she was feeling quite well with some improvement in her exercise tolerance. She still had pain on exertion, worsened by trinitroglycerin, with faintness, dyspnoea, palpitations, and a feeling of agitation relieved after a varied period by rest. A cardiogram again showed a 2:1 heart-block on exertion. When the exertion was more strenuous, alternate P waves were buried in the T waves, making it possible to miss the 2:1 block (see Fig. 2 c). On this occasion less strenuous exercise caused the symptoms to be less severe and the tracing showed separation of the T and P waves (Fig. 2 d).

On May 28 her exercise tolerance had improved further. A cardiogram showed that she was in sinus rhythm. As soon as one tablet of trinitroglycerin was completely dissolved in the mouth, a 2:1 block occurred with palpitations but no other symptoms. On dressing, the pulse rate fell to 40 and she felt faint. Five minutes later the rate had returned to 72.

Case 3

A housewife aged 67 was admitted to Charing Cross Hospital on January 4, 1962, for cholecystectomy. She had suffered symptoms of gall-bladder disease for 23 years. The gall-bladder was thickened and full of stones. She made an uneventful recovery from the operation and lost her digestive symptoms.

On May 21 she was admitted to the medical ward with a five-weeks history of faintness on exertion, pain across the chest and down the arms, dyspnoea, and pain in the legs. On two occasions consciousness had been lost. Swelling of the ankles occasionally occurred. The pulse was 50 and regular, the blood-pressure 250/80. A systolic murmur was heard over the praecordium, maximal at the apex. There were no signs of failure. A cardiogram showed a 2:1 block (Fig. 3 a).

The patient was admitted to hospital and a cardiogram done the next day, when the rate was 60 and irregular, showed a complete heart-block with beats arising from many ectopic ventricular foci (Fig. 3 b). Trinitroglycerin caused the rate to fall to 45 and the rhythm to become regular with a 2:1 block (Fig. 3 c). Exercise caused pain in the chest and the cardiogram now showed a complete heart-block with a ventricular rate of 30 (Fig. 3 d). With rest the pain subsided and the 2:1 block returned (Fig. 3 e). A similar sequence of events recurred when the experiment was repeated two days later.

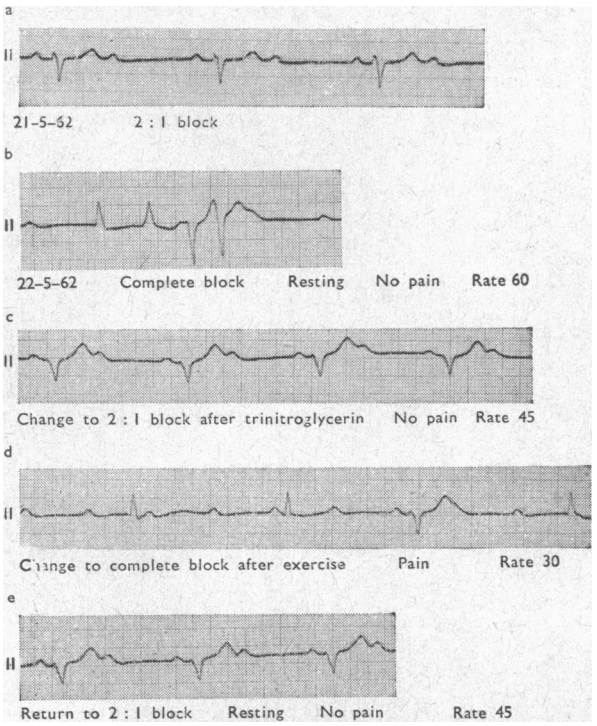

FIG. 3.—Case 3. Cardiogram showing changing heart-block with effect of trinitroglycerin and exercise.

Case 4

A bill-poster aged 65 was admitted to Charing Cross Hospital on March 27, 1956, after collapsing outside the hospital with severe dyspnoea and faintness but no loss of consciousness. A similar episode lasting a few hours but associated with severe pain occurred three weeks before admission.

On admission the pulse rate varied between 50 and 60. There were signs of left ventricular failure, confirmed by a chest *x*-ray examination, and right ventricular failure with pitting oedema of sacrum and ankles. A cardiogram showed a complete heart-block with a rate of 50 (see Fig. 4 a).

The day after admission the pulse rose from 50 to 68, the dyspnoea completely subsided, and the patient felt much improved. Two days later he became acutely dyspnoeic with a fall in the pulse rate to 44. He complained of a pain in the chest and coldness in the legs at this time. His condition continued to fluctuate in a remarkable way. On April 19 he suddenly sprang out of bed, disorientated and unable to speak. On May 14 the pulse was 80 and regular. There were a few rales at the lung bases but no peripheral oedema.

He was discharged from hospital but readmitted on June 9 with a three-weeks history of pain in the chest and dyspnoea on exertion. The pulse was 48 and the blood-pressure 195/80. There were now no signs of congestive failure, and a cardiogram done two days later showed a 2:1 heart-block (see Fig. 4 b).

He was readmitted on July 30, 1956, with a recurrence during the previous week of transitory loss of consciousness, with severe retrosternal pain on exertion and marked breathlessness. On admission he was dyspnoeic at rest, the pulse was regular and the rate 40. The blood-pressure was 210/80. Adventitious sounds were heard in the chest, the jugular venous pressure was increased, and there was oedema. He felt better and discharged himself two days later.

It seems that he did not attend hospital again until two years later, when he was admitted to another hospital on June 30, 1958, and died the following day. A severe cardiac infarction was found on post-mortem examination.

Discussion

Pain, dyspnoea, palpitations, faintness, weakness of the limbs, and alarm due to an increasing heart-block on exertion are a syndrome which is probably common but has remained unrecognized for a number of reasons. First, patients who complain of so many symptoms may be regarded as neurotic. Furthermore, the pain does not have all the characteristics of effort angina. Some days, when the heart-block is stable, exertion will not produce symptoms. On other days, when the condition is

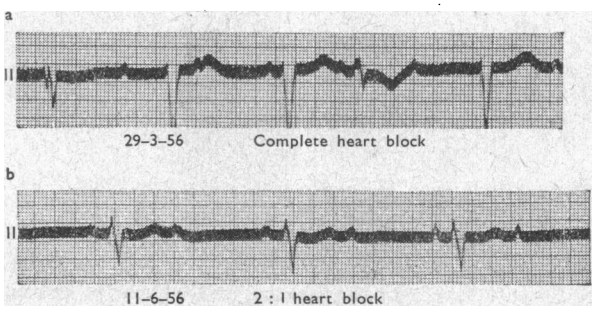

FIG. 4.—Case 4. Cardiogram showing unstable heart-block.

labile, the exercise tolerance may be severely limited. The pain is not always immediately relieved by rest, since this relief appears to depend on the return of the heart-block to the resting state. Similarly, the pain may occur at rest with the abrupt slowing of the heart rate due to the onset of heart-block. The history may be very suggestive of an impending cardiac infarction. When the change is from 1 : 1 to 2 : 1 block a cardiogram will not be helpful between attacks, and the fear that the symptoms are due to an impending cardiac infarction will prevent an exercise test being done. Some of these patients must be undergoing treatment with continuous anticoagulants and unnecessarily running the hazards of this therapy. A 2 : 1 block might be missed when alternate P waves are buried in the T waves as in Case 2 (Fig. 2 c). The feeling of panic, probably a manifestation of left ventricular failure (Fowler, 1962), also suggests a psychogenic basis for the symptoms.

The symptoms in patients with a transient or changing heart-block vary from typical Stokes–Adams attacks on the one hand to the unrecognized chest pain and other symptoms described here. When chest pain occurs in a patient with heart-block it is assumed to be anginal and the pain and the block are attributed to ischaemic heart disease. Smith and Zoob (1961) have shown that many cases of heart-block in elderly persons are not due to ischaemia, the cause being unknown. One of the four cases described had clinical evidence of coronary artery disease and another had post-mortem proof. But it cannot be assumed that the heart-block in these patients was due to ischaemia. The chest pain was clearly related to the heart-block itself and not to any coronary disease that might also be present.

Froment *et al.* (1959) state that the pain is anginal because of the characteristic features, particularly the relief with trinitroglycerin. The effect of trinitroglycerin is mentioned only in their patient in whom some ischaemic heart disease was found at post-mortem examination. Assuming that the pain is due to decreased coronary blood flow with the onset of heart-block (Starzl *et al.*, 1955), there is no reason to believe that a coronary vasodilator should be beneficial in such a case. Trinitroglycerin may cause the heart-block by accelerating the auricular rate and thereby produce or aggravate the pain as seen in two of the four cases reported here. Similarly, effort angina due to anaemia may be worsened by vasodilators (Fowler, 1962). Evidence that the pain in these patients is not due to cardiac anoxia stems from observations on Case 1. A 2 : 1 block produced by slight exertion caused severe symptoms but no ischaemic changes in the cardiogram, whereas later severe exertion producing a definite ischaemic pattern was associated with only slight retrosternal discomfort. The abrupt slowing of the heart at the time of increasing venous return with exercise could lead to distension of the heart. This was considered to be the possible cause of the pain in these patients before discovering that many years ago Pierre Merklen (1908) attributed angina pectoris to sudden left ventricular distension.

The other symptoms associated with the chest pain can be attributed to the abrupt slowing of the heart when exercise is increasing the venous return. It has often been shown that adaptation to heart-block occurs so that the working capacity becomes virtually normal (Gilchrist, 1934 ; Campbell, 1943 ; Ikkos and Hanson, 1960), but there is no time for adaptation with the transient changes in rate described here.

Summary

This paper describes the cases of four patients with a syndrome in which chest pain, dyspnoea, palpitations, faintness, weakness of the limbs, and alarm are associated with a transient or increasing heart-block occurring usually on exertion. The symptoms may occur at rest and may be aggravated by trinitroglycerin.

This syndrome is probably common, but the symptoms are attributed to a psychoneurosis or an impending cardiac infarction. The diagnosis is confirmed by a cardiogram taken after exercise. This may be considered unnecessary if the patient is thought to be neurotic, and dangerous if an impending cardiac infarction has been diagnosed.

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TREATMENT OF EXACERBATIONS OF CHRONIC BRONCHITIS WITH AMPICILLIN

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Several different antibiotic regimes have been proposed for the treatment of exacerbations of infection in patients with chronic bronchitis. These antibiotics have been chosen for their activity against *Streptococcus pneumoniae* and *Haemophilus influenzae*, which in the past ten years have become recognized as the common pathogenic organisms isolated from the sputum in an exacerbation (Mulder *et al.*, 1952 ; May, 1953). *Str. pneumoniae* is sensitive to a variety of antibiotics, but it is more difficult to select a suitable antibiotic with activity against *H. influenzae*. Benzylpenicillin is effective only in large doses (Goslings *et al.*, 1961). The acid-resistant penicillins with a phenoxymethyl, phenoxyethyl, phenoxypropyl, or a phenoxybenzyl side-chain show less activity against *H. influenzae* than does benzylpenicillin (Barber and Waterworth, 1962). Streptomycin is effective and bactericidal but has the disadvantages of having to be injected, the possibility of masking pulmonary tuberculosis, and the risk of eighth-nerve injury. The tetracyclines are effective against most strains of *H. influenzae* but are only

*Working with a reseach grant from Beecham Research Laboratories Ltd.