CERTAIN OPERATIVE PROCEDURES ON THE NECK

CONSIDERED FROM

A CARDIOLOGICAL STANDPOINT.

BY

IAN G. W. HILL,
M.B., Ch.B., M.R.C.P.

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INTRODUCTION.

A notable feature of the surgery of these latter decades has been the increasing degree of co-operation between physician and operating surgeon, a co-operation that has benefited both partners in the alliance, and has led to undoubted advances in the art of Medicine, using the term in the comprehensive sense. One may trace the existence of this alliance to-day in many fields of surgery and medicine: in this thesis one proposes to deal with one such - that of the surgery of the neck from the point of view of the cardiologist.

In the course of an investigation upon the physiological functions of the Carotid Sinus in the neck and their relation to the regulation of the heart-beat, it has become more and more evident that these have for the surgeon operating in that region a definite interest. Not only are these structures exposed and stimulated in the course of many surgical procedures, for excision of cervical glands and such like, but in various continental schools operations for the relief of certain cardiovascular diseases have been based on the denervation of these organs. Enthusiasm has been carried so far in some cases as to lead to operation on the sinuses in cases of epilepsy and dementia - an enthusiasm which can only /
only be described as at once excessive and mis-
guided. In view of the comparative novelty of the
subject a review of the present state of our know-
ledge and the presentation of certain personal
experimental observations made on man and on
animals may however be not inopportune.

A comparatively recent development in the
surgery of the neck has been the introduction of
operative procedures on the extrinsic cardiac nerves,
designed to cure or to alleviate the condition of
angina pectoris. This may be regarded as but a
branch of the new 'surgery of the sympathetic
nervous system', but cardiac innervation and
cardiac disease are alike so complicated, so
indefinite, and the subjects of such controversy
that one feels justified in treating them as a
special field. Personal research on this subject
one has none to report, but the surgery of angina
pectoris plays too large a part in the matters
embraced under the title of this paper to be ignored.

The surgery of toxic goitre has for one
interested in cardiac disease a very particular
interest. One is interested in the course of the
cardiac manifestations of thyrotoxicosis after
operation, and in the reaction of the damaged
hearts to the strain of the 'hyperthyroid crisis'; both /
both are matters that have attracted a great deal of attention in recent years. Further, one is interested in the actual response of the heart to the operation itself: to anaesthesia, to operative interference with the gland, or to the cardiac nerves around it. As this last aspect has principally engaged one's attention, one will discuss it and bring forward such observations as are relevant.

With so much by way of introduction one may proceed to define the scope of this paper, and to outline the plan to which it is drawn. With actual surgical technique one is not competent to deal, nor is such matter relevant here. Attention will be devoted to the consideration of the anatomical and physiological facts which form the basis for various operations, and which serve to explain certain observed effects, and to the presentation of such personal observations as exemplify various points of interest or importance.

The paper will be divided into five sections, each dealing with a limited field of the subject, namely:

I. Angina Pectoris: a brief survey of aetiology and pathology with a consideration of the anatomical basis for various operations recommended and practised.

II /
II. Carotid Sinus and Glomus Caroticum: a review of the anatomy and physiology of these organs.

III. The Surgery of the Carotid Sinus and Glomus Caroticum: with two sections dealing respectively with the observations on the function of these organs in man made by various surgeons, and with the role of the sinus in pathology and applied surgery.

IV. Some Observations on the Heart during and after Goitre Operations: in this section will be discussed the reaction of the heart to the actual operation; the post-operative course of the cardiac manifestations; certain unusual post-operative complications; and the role of drugs such as digitalis, quinidine and ergotamine in post-operative treatment.

V. The Action of Anaesthetics on the Heart, in so far as these have a bearing on neck surgery: a brief review of previously published cases together with personal records of several cases will be given.
I

ANGINA PECTORIS.

Consideration of this subject falls naturally under the following heads, which will be dealt with seriatim:— (i) Aetiology of angina pectoris. (ii) Anatomy of nervous paths concerned. (iii) Types of operation practised. (iv) Results of operation. (v) General discussion.

(i) Aetiology. Some knowledge of the causation of the syndrome known as angina pectoris is an essential for the surgeon who attempts to treat the condition, and it is here that the physician ought to be able to afford valuable aid. Unfortunately there is no agreement among cardiologists as to the causation. Several views are current, each supported by a wealth of assertion but by little actual proof. There are three main theories in vogue, all of which merit consideration; two of these are associated with the names of British physicians - ALBUTT and MACKENZIE - while the other is the product of a continental school headed by DANIELOPOLU, of Bucharest.

ALBUTT(2) thought that the pain arose from the aorta: the aortic blood pressure distending diseased areas caused the pain. Areas of inflammation would be especially susceptible, and anything raising the aortic blood pressure would tend to precipitate an attack.
attack. In this way he explained the known association of angina pectoris with aortic disease (e.g. aortic incompetence) and with such precipitating factors as emotion, exertion and exposure to cold with peripheral vaso-constriction. Death in an attack was, he thought, due to vagal action, and hearts the seat of advanced myocardial disease would be the most likely to stop under vagal stimulation. The absence of angina after heart failure set in was due to inability of the failing muscle to raise the aortic pressure to a sufficiently high level.

In this connection it is well to stress the work of those later writers (WENCKEBACH, REID, et al) who emphasize the role of the depressor mechanism which normally lightens the load of the heart in times of stress - the aortic reflex through the depressor nerve of CYON. These writers state that in failure of this reflex, whether central or peripheral, angina pectoris results.

The view of MACKENZIE(43) is summed up in his own words: 'The pain of angina pectoris can best, for practical purposes, be considered as an expression of exhaustion of the heart muscle, generally from insufficient blood supply'. He stresses the importance of defects of the coronary circulation as the cause. The association with effort /
effort is explained through relative inadequacy of a previously barely adequate blood supply through increased demands of the active muscle. MACKENZIE also emphasises the importance of the individual make-up in the production of the pain of angina. Some people have a nervous system which is abnormally sensitive to stimulation ....... The recognition of the hypersensitive nervous system is essential to diagnosis and prognosis in angina pectoris'.

The third view, that of DANIELOPOLU and his collaborators, tends to link MACKENZIE'S theory with the known facts of coronary disease. The essential point in this view is the hypothesis of a reflex, the 'pressor circle reflex', which acts through nervous channels somewhat in the following manner. In a heart, the seat of angina, various 'predisposing factors' may be at work - obstruction of the mouths of the coronary vessels, abnormal vaso-constrictor reflexes in the general or coronary circulations, with possible hyperexcitability of the sympathetic and visceral sensory systems - while the onset of an attack is determined by the action of such a 'determining factor' as increased work of the heart or decreased blood supply to it. When an attack supervenes, the insufficient blood supply causes /
Fig. 1: Scheme of Cardiac Innervation, after DANIELOPOULU.

(Zeits. f. klin. Med., 1930, CXIII, 294)
causes accumulation of fatigue products in the muscle, causing excitation of sensory endings in the muscle, and setting up a series of sympathetic reflexes - the 'pressor circle reflex' - which maintain the pain after the exciting factor has disappeared. This conception of a reflex is necessary to the understanding of his operative treatment for the condition.

(ii) Anatomy of nervous paths. Here again we have no agreement among anatomists or physiologists or surgeons. Two figures are reproduced, one from DANIELOPOLOU (13), and one from SWETLOW (61), which show sufficiently well the complexity of the cardiac innervation and the lack of agreement on essential points.

The two anatomical problems requiring solution are (1) what are the nerves whose integrity is essential to the proper function of the heart; and (2) what are the afferent paths for pain sensation from the heart. François Frank showed in 1889 that in animals a considerable proportion of sensory fibres from the heart run via the cervical sympathetic chain, and especially through the Stellate ganglion; and others run via the vertebral nerves. These experimentally established facts are the grounds for JONNESCO's operation. (vide infra).
Fig. 2: Scheme of Cardiac Innervation, after SWETLOW.
(Am. Heart Jour. 1926, I, 393)
In Vienna, WENCKEBACH recommended, and two surgeons executed, division of the 'nerve of CYON' in man. The depressor nerve or nerve of CYON in some animals runs as a separate strand from the arch of the aorta to join the vagus at a high level. In others (dog, cat, and probably also man) it usually runs its course incorporated in the vagus trunk. Its function is to transmit afferent impulses from the receptor organs in the adventitia of the aortic arch, which play upon the centres for the regulation of heart rate and blood pressure. Stimulation of the depressor nerve by a rise in aortic blood pressure causes cardio-inhibition and a peripheral vaso-dilatation. This nerve may or may not transmit sensation, such as is demanded by ALBUTT's theory. In some cases in man a nerve has been described which has connections with the vagus trunk, and with the superior laryngeal branch of that nerve; this may represent the depressor nerve of such animals as the rabbit. It is very inconstant, its anatomy is almost unknown, and its function problematical; even if it be a true depressor its section is a matter of doubtful advisability (see (v) infra.). SWETLOW gives a different course for the aortic nerves in his plate (q.v.).

Another point of prime importance, and of equally /
equally little certainty to the last, is the course of the cardio-accelerator fibres in man. DANIELLOPOLU shows them as running mainly from the second, third and fourth Dorsal roots to the Stellate ganglion, but other surgeons either ignore the point or contradict him. DANIELLOPOLU attributes the dangerous sequelae of JONNESCO's operation to division of these vital fibres, and has modified his operation accordingly. (see below).

(iii) Types of Operation. These may be grouped according to the severity of the measures employed as (a) radical, and (b) palliative. (In the strict sense of the term all are of course merely palliative measures). In the first class, the pioneer was JONNESCO(36), who practised excision of the cervical sympathetic chain for various disorders, including angina pectoris. Here also epilepsy figures in the list of 'indications' for the operation: in the employment of a surgical measure for the cure of epilepsy one finds an index of enthusiasm run riot, whether it be JONNESCO with his cervical sympathectomy, or JACOBOVICI and his co-workers with their excision of the glomus caroticum. The other main advocate of radical measures is DANIELLOPOLU(13), who practises an operation he terms 'the suppression of pressor reflexes' /

**Fig. 3:** Scheme of DANIELOPOLU's operation.  
*(Zeits. f. klin. Med. 1930, CXIII, 294)*
resembles that of JONNESCO, but has important modifications. In the first place, he spares the Stellate ganglion on account of the cardio-accelerator fibres, and secondly, he severs all centripetal fibres running to the vagus. In his own words:


(The fibres forming the anastomosis between vagus and superior laryngeal, which as implied above are not always present, appear to form part of the depressor nerve' connections of other authors).

These two operations, with various modifications, are practised extensively on the continent and in America, but have little vogue in this country. The operation of division of the 'depressor nerve' has already been referred to. It is seldom practised as a separate procedure, but forms a part of DANIELLOPOLU's complete operation.

As an example of less radical measures, one
may cite the paravertebral injection of alcohol into the ganglia of the chain: this is, however, outwith the scope of this paper, and the reader is referred for details to the article by SWETLOW. (61).

(iv) Results of Operation. Briefly, as reported these are less disappointing than one would have anticipated from the nature of the disease, and from the uncertainty of the methods employed. It is claimed that in successful cases the incidence of attacks is lessened or abolished, and that the patient passes the rest of his days in comfort. It is to be noted, however, that fatal results have followed operation, and in some cases appear to be attributable to the operative procedure employed, (e.g. asystole after JONNESCO's operation, etc.) In a case recorded by LEVINE(39) where superior and middle cervical ganglia were excised on both sides for goitre, auricular fibrillation supervened forty-eight hours later, and death from hyperthyroidism occurred some months later. In all cases of cervical sympathectomy one has the inevitable sequel of HORNER's syndrome, with ocular and cutaneous signs due to cervical sympathetic paralysis. The most comprehensive review of the operations and their results with which one is acquainted is that by McCULLOCH(44).
(v) Discussion. We are here rather in the position of 'infants crying in the dark'. Our knowledge of angina and its causation is little; our knowledge of cardiac innervation in man is as scanty. We are uncertain which nerves transmit the pain sensation, and do not know what ill effects may ensue from section of fibres that play an important role in regulation of the heart beat. We may doubt whether the abolition of a warning signal (pain) is justifiable, even if feasible, for the patient may be deprived of the sole indicator which warns him that he has overstepped the margin of safety, and has exceeded in his demands the powers of the heart muscle. The operation of division of the 'depressor nerve' seems on theoretical grounds to be unjustifiable. If this nerve is an integral part of a safeguarding reflex, designed to protect the heart from over-strain, it is surely a priori wrong to divide the nerve and destroy the safety mechanism in precisely those cases in which it is most essential. It is perhaps fortunate that in general this nerve runs an obscure course, and is not easy either to identify or to divide. MACKENZIE\(^{42}\) sums up the position in masterly, if caustic, fashion when he says 'The knowledge of the functions of the vagus and sympathetic which the surgeon cuts is so imperfect /
imperfect that neither he nor the physician who advises him understands more than a fraction of the functions of these nerves'.

The more moderate advocates of surgical treatment emphasise that the results are at best palliative - the actual heart lesion being uninfluenced at best, or possibly worsened. One doubts whether it is justifiable to expose one's patient to the risk of such operations for a problematical symptomatic improvement, which may be definitely harmful so far as ultimate prognosis is concerned.
Micro-photographs x 10 from serial horizontal sections through the carotid bifurcation.
II.

THE CAROTID SINUS and GLOMUS CAROTICUM.

As in the case of the surgery of angina pectori one must here devote a preliminary section to the anatomy and physiology of the carotid sinus and its reflexes, before passing on to discussion of its role in surgery.

Anatomy of Carotid Sinus. By the term 'carotid sinus' is indicated the slight bulbous or fusiform dilatation seen (in man and various animals) at the origin of the internal carotid artery. This sinus or bulb is accurately figured in most anatomical textbooks, but is not usually described: its presence is easily verified at operation or post-mortem in a large percentage of cases, though the degree of dilatation present varies considerably. It occupies the first half inch of the vessel, and blends insensibly into the narrower calibre of the distal portion of the artery. The wall of the sinus is notably thinner than that of the remainder of the vessel. The low power microphotographs figured are from serial sections taken from the bifurcation of the common carotid artery in a dog, and illustrate this point. (Figs. 8 - 11) It will be noted that in this animal the internal carotid is relatively a small vessel in that portion of its course distal to the /
Fig. 4: Innervation of Carotid Sinus after HERING.

(Lovatt Evans, Recent Advances in Physiology, 1930).

Fig. 5: Innervation of Carotid Sinus after HEYMANS.

(Lovatt Evans, Recent Advances in Physiology, 1930).
Fig. 6. — Innervation of Carotid Sinus after DANILOPOULOU.
(Presse Med., Paris, 1927, XXXV, civ, 1565)

Fig. 7. — Innervation of Carotid Sinus and Body after DRUNER (Deut. Med. Woch., 1925, LI, II, 1559)
the carotid sinus, whereas at the origin, its
diameter equals or exceeds that of the external
carotid.

The innervation of the sinus is less simple.
The original description of its nerve-supply was by
HERING(29), who stated that it received a fine
filament from the ninth nerve, taking origin high
up the Glossopharyngeal trunk, and running in the
fatty and connective tissue of the space between the
internal and external carotids to reach the sinus.

The workers of the Belgian school (HEYMANS(31) and his
collaborators) describe in addition a branch arising
from the superior laryngeal branch of the vagus.
This nerve and its connections have been fully worked
out by DE CASTRO(15,16). A further addition has
been made by DANIELOPOLU and his co-workers(14), who
describe a twig from the superior cervical ganglion
of the sympathetic, as well as both of the nerves
described by HERING and HEYMANS(Fig.6). The painstaking
anatomical researches of DRUNER(17) in Quierschied
have certainly not simplified matters - he finds
connections with all three nerve trunks (vagus,
glossopharyngeal and sympathetic) and of a complexity
(Fig.7) that is best gauged from his figure. It is to be
noted that he traces these nerves mainly to the
Glomus Caroticum, and not to the sinus, which he says
is /
Fig. 12: Micro-photograph x 300.
Silver preparation from sinus of rabbit, showing nerve elements.

Fig. 13: Microphotograph x 300.
Similar preparations showing location of nerves in adventitia.

Fig. 14: Microphotograph x 300.
is poorly supplied with nerves.

A collection of highly specialised and abundant nerve endings in the wall of the sinus has been described by DE CASTRO, who looks upon these as receptor organs for the reflexes about to be described. These nerve endings lie in the adventitia of the sinus, are specially abundant in a certain well defined area, and are peculiar to the sinus part of the vessel. The glomus caroticum is similarly richly innervated, and also possesses specialised nerve endings. The micro-photographs reproduced are from sections cut from the region of the carotid sinus in the rabbit. The fresh tissue was fixed by the Chloral-Alcohol method, and staining was by silver impregnation in bulk. (method used by DE CASTRO). (Figs. 12,13,14).

The carotid body or Glomus Caroticum is a small organ, 'the size of a hemp-seed', oval, yellowish in colour, situated usually in the fork of the carotid bifurcation. It has a peculiar histological structure, characterised by large pale cells with a most complete vascular and nervous network that appears to ramify round every individual cell. Its innervation has already been considered.

The Glomus Caroticum has been for long a puzzle to anatomists and physiologists alike. It has usually /
usually been taught that it belongs to the system of chromaffin bodies - to be in fact a para-ganglion, analogous in development and function to the suprarenal medulla or to the glomus coccygei.

DE CASTRO (15) in 1924 drew attention to its extreme vascularity, and suggested that its probable role was that of an endocrine gland. Four years later (1928), in the light of the innervation that he had meantime described, and in the light of experimental work, he revised that opinion, (16) and now considers it an adjuvant to the carotid sinus, whose physiological role we will now briefly study.

Physiology of the Carotid Sinus. The investigation of the functions of the carotid sinus was originally carried out by HERING, who was led to consider the problem on clinical grounds. It had long been known that pressure over the vagus in the neck caused usually a slowing of the pulse, a phenomenon attributed by TSCHERMAK (1866) to direct stimulation of the nerve by the pressure. HERING (28) was struck by the fact that in some cases the lightest of touches with one finger over a certain spot in the neck could cause marked cardiac slowing, and he knew from animal experiment that direct pressure on the exposed vagus nerve caused no slowing of the heart. He concluded therefore that the /
the cardiac effect of so-called 'vagal pressure' was a reflex, and succeeded in demonstrating that it arose from the region of the sinus (1923).

HERING has made a very complete study of the reflexes concerned, and his work has been amplified by HEYMANS and his co-workers in Ghent. The reflexes originally described by HERING were the two elements of a complete 'depressor reflex': i.e., cardio-inhibition and vaso-dilatation resulted on stimulation of the sinus. The stimulus might be mechanical pinching, faradism, or the natural stimulus from within of increased pressure in the sinus. The effects produced were exactly analogous to the depressor aortic reflex through the nerve of CYON described under the section on angina pectoris. HERING demonstrated that the afferent paths were the sinus nerves, and the efferent paths the vagi and the sympathetic tracts in the cord. The vagal effect is homolateral, for division of the vagus on one side completely abolishes cardiac slowing on stimulation of the corresponding sinus; stimulation of the opposite sinus has the usual effect.

HEYMANS and his fellow-workers have performed a series of very beautiful experiments with crossed circulations in animals, proving that the blood pressure changes previously attributed to the activity /
activity of an hypothetical 'centre' in the medulla are due to reflexes from the sinus caroticus set up by changes in the pressure of the blood flowing through them. They have added to the original cardiovascular reflex a reflex regulation of respiration, and have shown that the sinus receptors are sensitive not only to the pressure of the fluid in the vessels, but also to its qualities - pH, CO₂ content, etc. (32, 33, etc.) They have in fact deprived the 'centres' for regulation of blood pressure, heart rate, and respiration of their attributed powers of discrimination of pH, pressure, etc., and have reduced them to mere central synapses in reflex arcs: according to these workers, the discriminating receptor apparatus is located in the walls of the carotid sinus, and possibly in the Glomus Caroticum. Various workers in this country have investigated the parts played by the medullary 'centres' and by the carotid sinus and aortic reflexes in the regulation of the circulation. ANREP and SEGAL (4) confirming earlier experiments of ANREP and STARLING (5), find that the heart rate is influenced directly by the blood-pressure in the brain, and also by the aortic pressure. On the other hand, FLOREY, MARVIN and DRURY (23) state from their work on dogs, cats and rabbits, that their experiments 'preclude the /
Fig. 15: Mechanical Stimulation of Sinus.

Kymograph tracing from cat: $\times \frac{3}{4}$.

From above downwards, auricle, ventricle, femoral blood pressure, signal, and time marker in 10".
the assumption that the nerves of the cerebral vessels are of an afferent nature subserving a depressor reflex'. An intermediate position is taken up by Nash(46), who while admitting the part which the sinus may play in this regulation states 'However the effect of changes in blood pressure in the head must be considered to depend not only upon a reflex from the sinus caroticus, but also upon another more central effect'.

Danielopolu has added visceromotor reflexes to the list by demonstrating gastric hypermotility in man on stimulation of the sinus(14).

We are here concerned only with the original reflex of Hering. This one may repeat is exactly analogous to the aortic depressor reflex of Cyon, and has for its function the regulation of the cerebral blood pressure. It is capable of being set free not only by changes in the blood pressure in the sinus, but by mechanical stimulation of the sinus wall from without.

The tracings reproduced in figures 15 - 20 are from experiments performed personally on various animals in the Department of Physiology, working in collaboration with Mr. W. A. Bain, B.Sc., F.R.S.E., Assistant there.

In figure 15 is shown a tracing from a cat under /
Fig. 16: Electrical Stimulation of Sinus.

Kymograph record from rabbit: x ½.

From above downwards, auricle, ventricle, femoral, blood pressure, signal and time marker in 10".
under urethane in which the exposed carotid sinus was pinched with fine dissecting forceps. The tracing shows marked cardio-inhibition, with a slight fall in the blood-pressure. There is a noticeably long latent period before the latter effect appears, and the fall in blood-pressure occurs well in advance of the heart slowing.

Figure 16 shows a similar tracing from a rabbit, also under urethane, in which faradic stimulation of the sinus was employed. In this case the cardio-inhibitory action is slight, but the fall in blood-pressure is much more marked than in the last case. Measurement on the original tracing shows the fall to be from 80 to 48 mm. Hg., while the heart rate slowed from 198 to 180 per minute. With pressure on the sinus with forceps (lateral pressure only without pinching) the blood-pressure fell over 20 mm. Hg., while the heart rate remained constant at 204 per minute. The magnitude of the fall in blood-pressure in this experiment may be attributed to the enhanced reflex effects on blood-pressure described in the rabbit under urethane by FLOREY and MARVIN(22). No other experiment in our hands has yielded such marked results.

In figures 17 and 18 are shown two tracings from a dog, a decerebrate preparation; stimulation of the sinus /
Fig. 17:  
Electrical Stimulation of Sinus in Dog.  
Kymograph tracing of B.P. (x 11/12).  
Coil at 9 c.m.

Fig. 18:  
Same animal. Left Common Carotid occluded at "L.C." Sound introduced into Right carotid sinus at signal: sound withdrawn and left carotid freed at "O.L.C."  
Kymograph tracing of B.P. (x 11/12).
Fig. 19: Kymograph record of B.P. and Respiration.
Dog: x 2/3.
At signal, stimulation of sinus from within by sound.

Fig. 20: Kymograph record of B.P. and Respiration.
Dog: x 2/3
At signals, stimulation of vagus and of sinus with same strength of faradic current.
sinus with faradic current provoked a marked fall in pressure, while stimulation mechanically of the sinus wall from within, by a probe introduced through the common carotid, caused quite a noticeable drop in blood-pressure. The initial rise in the blood-pressure in the second tracing, before the introduction of the sound, is due to the clamping off of the left (opposite) common carotid: this causes a fall in the local pressure in the left carotid sinus, with consequent reflex rise in general blood-pressure. It is in fact an example of the normal physiological stimulus which calls forth these reflex changes in blood-pressure.

The last pair of figures (19 and 20) are from another dog, where the respiration was recorded as well as the blood-pressure. They show the effect on the blood-pressure of a probe introduced into the sinus through the common carotid: and the different effects of equal strength of stimulus applied to the vagus and to the carotid sinus on blood-pressure and respiration. The effects of sinus stimulation are similar to, but not so pronounced as, the vagal stimulation. The respiratory effect shows a tendency to persist longer with sinus stimulation.
III.

THE SURGERY of the CAROTID SINUS and GLOMUS CAROTICUM.

This subject is best considered under two heads:
(a) the observations on the function of these organs in man that we owe to various surgeons, and
(b) the actual operations performed on these organs for various diseases and disorders.

(a) Observations on their function in man.
A series of observations upon the cardiac aspect of the reflex from the sinus and the role of the vagus was commenced in Edinburgh in July 1930, a report on the results of which will be given below. This work was started in ignorance of the fact that somewhat similar observations on the vascular side of the reflex had already been carried out in various continental centres by several surgeons. It is therefore necessary to give first a review of their published reports in chronological order.

ENDERLEN (20), in June 1924 at Heidelberg, laid bare the bifurcation of the carotid in a case on which he was operating for goitre. He observed that compression of the sinus caused a fall in blood pressure from 105 to 67 mm Hg.

TILMANN (62), in November 1924 (? at Cologne), made similar observations on two cases. The first was a woman of 36, with a carcinoma of the lip and spread to the cervical glands: her blood-pressure before /
before operation was from 110 to 115 mm Hg., and 'vagal-pressure' over the intact neck gave no result.

At operation, the carotid sinus on the right side was compressed with the finger on three occasions, yielding a fall of pressure of 135 - 121, 135 - 123, and 135 - 125 respectively: it was noted that the pressure rose very slowly after the release of the compression, taking 40 seconds to reach its former level after a 15 seconds' compression of the sinus. The heart rate was but little affected. The experiment was repeated, using a 'Hopfner-clamp' as in animal experiments: this caused a fall from 132 to 112, and the heart action was also more marked. Compression of the left sinus caused a fall from 132 to 120 and from 132 to 122 on two occasions: it was noted that the pressure rose with the clamp still applied to 126 and 130 in the two experiments. A pull on the carotid trunk (common carotid) heartwards caused a fall in blood pressure to 110. The heart action was not observed during the operation on the left side.

TILMANN's second case was of a man, age not stated, with a left sided tumour ('Kiemengangzyste' - ? Branchial cyst) which lifted the carotid vessels forward, and was painful on pressure. The operation was under root anaesthesia: compression of the sinus with the finger caused a fall of pressure from 123 to 112 /
112 on two occasions, while the heart rate fell from 80 to 72. The application of a Hopfner-clamp caused a fall to 109 mm Hg., and the pressure rose more slowly than after finger pressure. It was noted when 'vagal pressure' was performed before the operation, that if pain was produced, the pressure rose instead of falling.

BOHNENKAMP (6), working in ENDERLEN's clinic, reported two further cases in 1925. Both were goitres, one between 30 and 40, and one over 40 years old. In the first, pinching of the right sinus with forceps repeatedly caused a fall in pressure of from 12 to 16 mm Hg., while the heart rate slowed by 10 to 20 beats per minute. Pinching of either vagus had not these results. In the second case pinching of the right sinus caused a fall of only 5 to 8 mm Hg., while the heart slowed by over 10 beats per minute.

ENDERLEN and BOHNENKAMP discuss also the much greater fall produced in their first case in 1924 (see p. 24), and seem to attribute the effect to various factors, including the anaesthetic: they state, however, 'Ob die Tiefe der Narkose einen Einfluss hatte, lässt sich nicht sagen und ausschliessen'.

BUDDE (7), working in the surgical clinic at Cologne /
Cologne, published reports of two cases in 1926. The following is an abstract of his paper.

Case 1: - man with carcinoma of lower lip, with involvement of cervical lymph glands of the right side. Local anaesthesia. Various manipulations around the carotid sinus called forth a well marked fall in blood pressure ...... from 153 to 126 with carotod-vagal pressure, and from 133 to 118 during dissection of the bifurcation of the carotid. A pull on the carotid with the finger caused a drop to 108, and the actual exposure of the sinus, a fall to 95 - 86 - 93. The passing of an aneurysm needle round the sinus with catgut caused a fall to 65, and with a Hopfner clamp the pressure fell to 72. (All figures are mm Hg.) The clamp seems to have been removed immediately, and the pressure rose at once to 108. Ligature of the superior thyroid artery and the superior maxillary artery caused a rise to 112: a pull on the bifurcation caused a fall to 85, with a succeeding rise to 90 - 112.

Case 2: - carcinoma of the cheek, with secondary glands on both sides of the neck. Two operations necessary, one to remove local growth and left side glands, the other for right sided cervical glands. General anaesthesia with ether. At the first operation on the left side, dissecting out the sinus nerve /
nerve caused a fall from 115 to 100 mm Hg. Section of the nerve was followed in a few minutes by a rise of pressure to 134. At the second operation the reflexes from the right side were investigated, with similar results. It was noted that pressure over the left sinus (denervated at previous operation) had now little effect, while the right had the usual action.

The author's summary is interesting, and will be quoted in full:

'The sinus-pressure experiments in man are definitely positive, and are more marked with local than with general anaesthesia: further it is to be noted that in exposing the region of the bifurcation of the carotid the same reflexes are set up, and the blood pressure falls. It falls to be emphasised that in the prophylactic ligation of the external carotid artery the bifurcation itself should be left quite alone, and the ligature passed at the level of the origin of the superior thyroid artery. So in the course of any neck operation, when a sudden fall in blood pressure occurs from any cause, it is possible to raise it by division of the easily found sinus nerve.'

At the clinic at Cluj, in Rumania, a certain amount of research on the functions of the Carotid Body in man has been carried out by JACOBOVICI, NITZESCU, and POP (1929)(34), in the course of which they investigated also the reflexes from the carotid sinus. In a previous paper (1928) NITZESCU and JACOBOVICI(49) published the results of an investigation of the susceptibility of the exposed human vagus nerve /
nerve to mechanical stimulation. In both series of experiments these authors seem to have employed methods that would hardly be tolerated in this country: they recorded the blood pressure in all their cases, for example, by introducing a cannula into the severed radial artery, and connecting it with a mercury manometer and kymograph as in animal experiments. This little operation, they naively remark, was performed under strict aseptic precautions and healing of the wrist wound was always by first intention. In their vagus experiments they employed faradic as well as mechanical stimulation, and went so far in one case as to cut one vagus, and 'stimulate' the ends by crushing in a Kocher artery forceps. Their results are interesting, but their methods are to be deprecated.

In the vagus investigation, four patients were 'operated' upon, three under general anaesthesia, one under novocain locally. They found that the intact vagus was capable of being stimulated by pressure between the gloved finger and thumb, and responded in marked fashion to pinching with dissecting forceps. The response was a 'complete depressor effect' - i.e. a fall in blood pressure accompanied by a cardiac slowing. In all cases but one the effect was slow to develop, and slow to pass off. From their tracings /

Die zweite Kurve der Abbildung bildet die direkte Fortsetzung der ersten.

Fig. 23.


Fig. 24.

Figs. 23 & 24: - Experiments on Vagus Stimulation (mechanical) in Man.

after JACOBOVICI and NITZESCU.

(Zeits. f. exper. Med. 1928, IXIII, 767).
tracings (Figs. 23 and 24) it can be seen that the stimulus was applied for about 20-30 seconds: the fall in blood pressure starts about ten seconds after the commencement of the stimulus, reaches a maximum in about thirty seconds, and passes off after about a minute. From the results in the case where the vagus was divided, they conclude that the effects are reflex in nature. In this case they found that stimulation of the distal (cut) end of the vagus trunk caused no effect, even on crushing with Kocher forceps. The usual dissecting-forceps pressure on the central end, however, caused a typical fall in blood pressure. (See reproduction). The authors conclude from their results that in spite of the possibility of setting free a depressor effect reflexly through stimulation of the vagus mechanically the pressure required is far in excess of that which can be employed clinically in 'vagal pressure', and conclude that HERING is correct in attributing the results of vagal pressure to a reflex, from the structures in the region of the carotid bifurcation.

In their second paper, these workers report six observations made on five patients, all between 20 and 30 years of age. Similar technique was employed to that described above, while actual removal of the Glomus Caroticum was carried out for various /


Fig. 21.

Fig. 22.

Figs. 21 & 22: Experiments on Carotid Body Stimulation in Man.

after JACOBOVICI, NITZESCUC, & POP.
(Zeits.f.d.g. exper.Med. Berlin, 1929,IXVI,359)

Experimentelle Untersuchungen über die Physiologie der Carotisdrüse beim Menschen.
various therapeutic indications which will be discussed later. They found that in all cases mechanical or electrical stimulation of the sinus caused no effect, while similar treatment of the carotid body caused a marked depressor result. The response to electrical stimulation (faradism) was so marked and constant, that they employed a 'seeking electrode' in searching for the carotid body in those cases where it could not be found by simple inspection. When a piece of tissue in the carotid fork was found which gave a depressor response, it was excised: they state that subsequent histological examination always revealed the typical structure of carotid body tissue in the tissue excised. They found a post-operative rise in pressure lasting many days after excision of the Glomus Caroticum. And they conclude "The reflexes hitherto described as 'carotid sinus reflexes', especially the depressor carotid sinus reflex of HERING, appear to arise through the mediation of the Glomus Caroticum, which would thus be the receptor-organ for the reflexes arising in the region of the carotid bifurcation. This reflex would thus be rather a carotid gland reflex than a carotid sinus reflex, and would have a part in maintaining the blood pressure at a normal level."

From /
From these abstracts of published cases one may note that first, the number of cases examined is not large, there being only seven German cases, and four 'vagal' and five 'glomus' cases reported from Rumania. It is possible that several of the cases in the last two groups may overlap, but in any case the number examined does not exceed sixteen.

Generally the observations have been made by Riva-Rocci sphygmomanometric readings of the blood pressure, and by counting of the pulse. In the Rumanian cases graphic records of the blood-pressure and pulse rate have been obtained.

Working in the wards of Professor D.P.D. WILKIE, in the Royal Infirmary of Edinburgh I have been able to investigate the sinus reflexes in seven cases. That this has been possible is entirely due to the courtesy and help afforded by Professor WILKIE, who in each case has interrupted the course of his operations on a busy morning to dissect out the sinus and stimulate it while records were being taken. Records have in all cases been made by the electrocardiograph, in order (a) to secure permanent records and (b) to study the actual cardiac mechanism involved in the cardio-inhibition observed. HERING noted in some of his animal experiments that the heart action was disturbed by more than a mere bradycardia.
bradycardia: accurate analysis of the disorder from kymograph tracings is not possible, and the precise knowledge afforded by the electrocardiograph is of inestimable value in such an investigation. There is, so far as one can trace, only one reference to the electrocardiographic changes in relation to carotid sinus stimulation, a paper by REGNERS (52), working exclusively with animals. In man the problem has not so far been studied. The method has the added advantage that records can be taken without interfering in any way with the aseptic technique, and with a minimum of disturbance to the operating surgeon. The blood pressure aspect of the reflex has not been observed: Riva-Rocci readings in a busy theatre can not be relied on to an accuracy of a few millimetres, and the fall produced does not seem to be of a high order: further, after several weeks' experimenting and search, no satisfactory method of continuously recording blood pressure from the intact brachial artery could be found. (The method adopted by the Rumanian workers was not even considered; its use cannot be justified.)

The protocols of the seven cases are as follow:

CASE /
Fig. 25:-- Case I. Electrocardiograms, lead II x 1/3 approx.

(i) Right caroto-vagal pressure under Chloroform.
(ii) Right sinus stimulation under Chloroform.
(iii) Right vagus stimulation under Chloroform.
(iv) Control one week later.
Caroto-vagal pressure after atropin.
CASE I. A.B., male, aet. 61 years.

Radical operation for malignant glands in neck, right side. Pre-operative dose of atropin, gr. 1/100th hypodermically. Chloroform anaesthesia. (Fig.25)

Control electrocardiogram at 12.25 p.m. with patient in the surgical stage of anaesthesia. This record shows regular rhythm at 108 per minute. The only abnormality is the absence of auricular deflections - "P" is isoelectric. At 12.27 p.m., pressure on the right side of the neck over the great vessels for six seconds on two occasions. This was not recorded.

Record resumed at 12.35 p.m.: "P" waves are now visible, positive and of good amplitude. The record now shows, however, another abnormality: the ventricular complexes are not all of the same type, but vary in alternating fashion. In one form (hereafter referred to as 'type I') the complex is essentially normal in appearance: QRS lasts 0.08 second, QRST - 0.32 second: P-R measures 0.16 second. The individual deflections measure (in millimetres) \( Q = -1, R = +12, S = -4, \) and \( T = +4. \) The type I complex is practically constant in its time-relations, and in its magnitude whenever it occurs. Not so with type II, which varies conspicuously in different parts of the record. In it, P-R varies from 0.08 to 0.12 second /
second, QRS is 0.08, and QRST is 0.28 second. Q is absent, R = +20, S is absent, and T = -5 mm. This is therefore a diphasic form of complex, such as is usually associated with ventricular extrasystoles or with bundle branch block. The short duration of QRS rule out the latter, while the short varying P-R intervals favour the supposition that these are extrasystoles. (Cf. the records under CHCl₃ anaesthesia on pages 76 et seq.) It is to be noted that the R-R interval is constant at 0.44 second independently of the type of complexes.

The exercise of pressure over the right carotid sinus (in the intact neck) caused no slowing of the heart rate, but caused a marked exaggeration of the size of the 'type II' complexes: a regular alternation of normal complexes with wide biphasic extrasystolic complexes is notable in the accompanying figure (25,i).

12.57 p.m. Resumption of the record. (Fig.25,iii) Meantime the neck had been opened, and the dissection of the glands on the right side partially carried through. The carotid arteries and vagus nerve on that side had been exposed. The stimulation of the exposed and freed vagus nerve by pinching with dissecting forceps was now carried out and recorded. Before the stimulation, it will be noted from the reproduction of the tracing, all the complexes in the record /
QRS or in PR. After the stimulation of the nerve, which lasted six seconds, there occurs a latent period of about three seconds, and then type 'II' complexes appear, alternating with normal type 'I' complexes as in the last record. These type 'II' complexes are of large amplitude, as in those occurring after pressure over the region of the sinus in the intact neck: there is again considerable variation in the amplitude of these abnormal complexes. From an examination of the original film, it is seen that after 36 seconds had elapsed, only occasional complexes were of the abnormal 'type II' variety: and after 45 seconds no more are visible till the end of the record at 53 seconds.

About 90 seconds after the stimulation of the vagus nerve, when the effects of this experiment had completely worn off, the bulb of the right internal carotid artery was pinched lightly in dissecting forceps for six seconds. Only the end of this period (Fig. 25, i1) of stimulation is seen on the record. After a somewhat longer latent period than in the case of vagal stimulation the two types of complexes are again seen to alternate, more or less regularly: the effect is not so persistent as in other records, but comes and goes in erratic fashion - present for fourteen /
fourteen seconds, absent for three: present again for nine seconds, absent for three: again present for nine seconds, and so on: type 'II' complexes still appear, isolated here and there for as long as sixty seconds after stimulation of the bulb.

It is to be noted that the same effects in modified degree followed on stimulation of the exposed sinus, the free vagus nerve, and the application of 'caroto-vagal pressure' on the intact neck. In all, PR and RR intervals remained unaffected: in all, the type 'II' complexes appeared and were of great amplitude.

With a view to determining how far the unusual effects of 'vagal pressure' and of vagal stimulation in this case were due to the use of atropin and of chloroform, a control experiment was carried out a week later on the healed neck. Ordinary 'vagal pressure' was applied: then atropin was given in the same dose as before the operation (gr. 1/100th) and after half an hour, the caroto-vagal pressure repeated. It was found that the atropin did not diminish the typical response to 'vagal pressure' elicited on this occasion. The ventricular complexes were, and remained throughout, of type I', while the P-R interval did not alter. The R-R interval lengthened from 0.92 seconds before stimulation to 1.06 during
Fig. 26:— Case II. Electrocardiogram, lead II. x ½ approx. Records during operation.

Fig. 27.

Fig. 28.

Figs. 27 & 28:— Case II. Electrocardiograms, lead II Control.

Right and left carotid-vagal pressure three months later.
the pressure: after atropin the maximum R-R noted during the pressure was 1.16 seconds. (Fig. 25,iv)

The unusual effects of vagal stimulation in this case, which was in fact the first in which one had taken a record under general anaesthesia, were for long very puzzling. In the light of other records secured later under CHCL₃ anaesthesia, however, the effects are now attributed to that drug: further reference to this will be made under the section on 'anaesthesia'. (vide infra).

**CASE II.** R.G., male, aet. 47 years.

Radical operation for excision malignant glands, right side of neck. Atropin sulphate, gr. 1/100th at 11.30 a.m. (H.I.). Anaesthesia induced at noon with ethyl chloride, followed by open ether and later by intratracheal ether. Skin incision at 12.20 p.m. Some difficulty was experienced with the recording of the experiments, and various steps were 'missed', e.g. the results of occlusion of the common carotid, and of occlusion of the two branches (internal and external) simultaneously. Records were secured, (Fig. 26) however, and are reproduced here, of the effects of stimulating the right vagus nerve and the right carotid sinus in the same manner as in the last case. It will be noted that no effect whatever was produced in /
in either case.

An opportunity was later taken to record the effects of clinical 'caroto-vagal pressure' on this man: these likewise show no effect on stimulation over the great vessels in the neck. We are here dealing with a case with insensitive reflexes. (Figs. 27, 28).

**CASE III.** MRS. S., female, aet. 63 years.
Radical excision of malignant glands, right side of neck. Preliminary atropin (gr. 1/100th H.I.): anaesthesia induced with ethyl chloride and maintained with intratracheal ether.

In the course of this operation a number of records were made while various manipulations were carried out on and around the carotid sinus: for example, during clearing of the bifurcation of the common carotid, during traction headwards and heartwards of the common carotid artery, during occlusion of the common carotid trunk, during ligature of a vas vasorum of the sinus, with traction on that structure, during stimulation of the bulb with dissecting forceps and during similar stimulation of the free vagus nerve. These records show uniformly negative results: here again no demonstrable reflexes were present. (see Fig. 29).

**CASE /**
**Fig. 29:** Case III. Electrocardiogram, lead II. x 1/3 approx. Records during operation.

**Fig. 30:** Case IV. Electrocardiogram, lead II. x 1/3 approx. Records during operation.
CASE IV.  J.K., male, aet. 63 years.
Radical operation for excision malignant cervical glands, right side.  No preliminary atropin or other drug.  Anaesthesia induced with chloroform at 11.36 a.m. (See Fig. 57, infra.): later intratracheal gas and oxygen, with minimal quantities of ether.  Skin incision at 12.22 p.m.

Figure 30 is a reproduction of tracings secured during this operation. (These records were made some forty minutes after the skin incision). From it it will be noted that occlusion of the common carotid had no effect upon the heart rate. In the second tracing, however, the effect of sinus stimulation is seen to be well marked. With the signal indicating pressure on the sinus the heart is seen to slow markedly, while the P-waves disappear. Some slowing is noticeable for a few beats before the actual pressure was applied: during this time the forceps were laid by the surgeon gently against the wall of the bulb, in position for applying a pinch – and apparently even this minimal stimulation is enough to set free a moderate degree of cardio-inhibition. By contrast, the stimulation of the vagus nerve is without effect. (tracing iii).
Fig. 31: Case V. Electrocardiogram, lead II x 2/5 approx.
Records during operation.

Fig. 32: Case V. Electrocardiogram, lead II x 2/5 approx.
Control: carotid-vagal pressure on healed neck.
CASE V. D. McG., male, aged 66 years.

Radical operation for excision of malignant glands left side of neck. No preliminary atropin or other drug. Induction of anaesthesia with chloroform. (see page infra). Later, intratracheal gas and oxygen with some ether.

Figure 31 is a reproduction of tracings made during this operation. In the upper tracing, the lack of effect of occlusion of the left common carotid is shown. In the second (which occupies two lines) is seen the effect of sinus stimulation. At the first signal the surgeon stroked the left sinus lightly with his forceps; no effect. At the second, longer, signal the sinus was pinched with dissecting forceps. The R-R interval, which had been steady at 0.68 seconds, increased in the second cycle after the start of the pressure to 0.8 seconds, and rose as high as 0.98 seconds. On the cessation of the pressure, which was sustained for 6.5 seconds, the RR interval fell again to normal. It was noted that in this case the P-waves did not disappear as in some former records with right sinus pressure. The P-R interval remained constant at 0.2 seconds; and the amplitude of P did not vary. In the third tracing (fourth line) the left vagus nerve was pinched with dissecting forceps. After a latent period of three
or four cycles, the RR interval lengthened from 0.72 seconds to 0.8 seconds, and then to 1.04 seconds. Simultaneously the P-waves abruptly disappeared.

After three long diastoles, a ventricular extrasystole appeared, following a supra-ventricular complex at 0.4 seconds and followed by a normal complex with P-wave at 0.98 seconds interval. The stimulation was ceased after the first long diastole, and was of six seconds' duration. P-waves appeared in the third complex after the cessation of the stimulation.

This patient was electrocardiographed on 22, xi. 30, and a control 'carotio-vagal pressure' carried through. (Fig. 32).

CASE VI. W.R., male, aet. 63 years.
Radical operation for excision of malignant cervical glands, left side. No preliminary atropin or other drug: chloroform induction at 2.04 p.m., change to intratracheal ether at 2.19 p.m. After exposure of the left sinus and vagus nerve, at 2.31 p.m., these structures were stimulated as in the other cases by pinching with non-toothed dissecting forceps. (see Fig. 33). No effects are visible in the records: in both P was invisible before stimulation of the sinus or nerve; in neither was bradycardia produced.

The sinus was injected with local anaesthetic at 2.33 p.m., some 1% novocain being injected with a fine /
Fig. 33: Case VI. Electrocardiogram, lead II, x \( \frac{1}{3} \) approx. Records during operation.

Fig. 34: Case VII. Electrocardiogram, lead II x \( \frac{1}{3} \) Records during operation.
fine needle under the adventitia of the vessel. A further sinus stimulation at 2.57 was likewise without effect. (Fig. 33)

CASE VII. A.S., male, aet. 62 years.
Radical excision of malignant glands, right side of neck. Atropin, gr. 1/100th H.I. before operation. Induction of anaesthesia with chloroform (see under V, (Fig. 58) page 78). Anaesthesia maintained with intratracheal ether.

In the course of the operation the vagus and sinus on the right side were exposed, and stimulated by pinching: the common carotid was also occluded for ten seconds. The records reproduced in figure 34 show no significant change in the heart's action.

SUMMARY/
SUMMARY OF RESULTS.

Positive results on stimulation of the carotid sinus have been obtained in only three of seven cases investigated. In two cases a bradycardia resulted analogous to that seen on 'vagal pressure', in the third an abnormal response with disordered cardiac action appeared. In this last case, performed under chloroform anaesthesia, an atypical but similar response was obtained on applying 'vagal pressure' to the intact neck. The effect is thought to owe its bizarre nature to the anaesthetic (see also p. 76 - 77 where this is discussed). Reference is made by ROSKAM to the exaggeration of these reflexes under chloroform.

In the three cases yielding positive results on sinus stimulation, the vagus nerve was found to be mechanically excitable in two; in the third case its stimulation gave no effect although sinus stimulation gave a bradycardia.

In four cases vagus and sinus were alike insensitive to stimulation: for this there are three possible explanations.

(i) The reflex may have been abolished by atropin: but it is known that the dose employed (1/100th grain) did not abolish the reflex in for example case I, and two of the four cases had no pre-operative dose of the drug: /
drug: therefore one is justified in stating that the action of atropin is not responsible for the absence of the reflex in these cases.

(ii) The anaesthetic may have suppressed this along with the other reflexes. It is notable that all cases (four in number) performed under intratracheal ether were negative so far as sinus reflexes were concerned. One case under chloroform, and both cases under intratracheal gas and oxygen yielded positive results. That ether has a depressant action of the vagus nerve is a known physiological fact (KOBACKER and RIGLER(37). It may be that the same holds in man.

(iii) The reflex may be absent in some cases. That this is true is shown by the failure to elicit any effect with 'vagal pressure' in case II in the absence of such complicating factors as anaesthesia, atropin, etc. One notes in the surgery of these reflexes the same individual variation in response as is clinically familiar in the application of 'vagal pressure' in medical wards; not every person responds with bradycardia to pressure over the sinus or great vessels in the neck. The converse complementary syndrome of hyper-excitable reflexes /
reflexes has not been encountered in the surgical theatre. Such cases do occur in practice, and one would be interested to see the reaction in such cases to direct stimulation of the sinus.

It is to be noted that the patients operated upon form a strictly limited class: with one exception they were all in the seventh decade of life (actual ages 61, 47, 63, 63, 66, 63, 62 years). Further all were operated upon for excision of malignant glands. One would be interested in the reaction of patients of younger type – say the adolescent or young adult with glandular tuberculosis. Though all cases were advanced in years, in no case was a gross arteriosclerotic change in the vessel noted, such as is described by GOORMAGHTIGH. (24)
(ii) The role of the sinus in pathology and applied surgery.

(i) Permanent Hypertension: It has been suggested that in hyperpiesis the regulating mechanisms that normally maintain the blood-pressure at a healthy level are either out of action or perverted in function. These mechanisms are grouped by HERING\(^{(30)}\) as 'Blutdruckzüglers', and are in effect the aortic and sinus depressor reflexes. The known peripheral vasodilatation in cases of aortic incompetence suggests a possible intervention of the former set of reflexes: and that the carotid sinus may play a part is held by GOORMAGHTIGH\(^{(24)}\). This author has described thirty cases in which he has examined the carotid sinuses histologically in cases of hyperpiesis. Gross lesions appeared only in cases with much hypertrophied hearts, and especially associated with aortic atheroma, seldom with peripheral arteriosclerosis. With commendable sanity and moderation he emphasises that 'it would be utterly puerile to hold the sinus responsible for human arterial hypertension', but he suggests it plays a part in its production. He refers to the experimental production of arterial hypertension in animals by section of the nerve of CYON and the sinus nerves.

The surgical bearing of this work lies not in the suggestion that operative interference with the sinus is /
is desirable in these cases: it lies rather in the further evidence against the advisability of dividing CYON's nerve in cases of angina pectoris.

(ii) Permanent Hypotension: On the other hand, certain cases displaying persistent low blood pressure appear to have over-excitable carotid sinus reflexes. The de-nervation of the sinuses or excision of the Glomus Caroticum has been advocated as a means to combat this, and has been practised abroad. But, as most cases of low blood-pressure associated with clinical discomfort or disease are associated also with peripheral spasm (e.g. RAYNAUD's disease) one can hardly conceive that the sinus is there over-active. An active sinus causes vaso-dilatation, and to produce spasm some other factor must be present: RAYNAUD's disease, again serving as an example, is, as is well known, bound up with disturbances of sympathetic innervation and of calcium metabolism. One hesitates therefore to recommend operations on the sinus for this condition; and low blood pressure per se is less likely to cause trouble than the high blood pressure that might possibly follow the operation.

(iii) Transient Low Blood pressure during neck operations: BUDDE recommends denervation of the sinus should a sudden fall in blood pressure supervene during /
during a cervical operation. It would seem less radical, and equally efficacious, to secure the 'ausschaltung' of the reflexes by painting or injecting the walls of the sinuses with novocain, as suggested by HERING\(^{(29)}\). This, however, should seldom be necessary: — syncope is not a specially common occurrence in cervical operations as opposed to those in other regions, so the sinus cannot play an excessively important role in its causation. The abolition of the reflexes, temporary or permanent, might be advisable in cases known to have unduly sensitive reflexes; such cases do occur in medical practice, where a light pressure, with even one finger, on the skin over the sinus causes marked cardio-inhibition. These cases are commonest in the elderly with palpable arteriosclerosis of the sinus region. A preliminary test for undue sensitivity of the sinus is advocated by ROSKAM\(^{(54)}\) before all operations on the antero-lateral aspect of the neck.

(iv) Epilepsy, Dementia etc.:— In the search for the causal factor in such diseases as epilepsy probably every organ in the body has in turn been incriminated. The sinus caroticus is no exception. DANIELOPOLU considers the Glomus Caroticum the important reflexogenic organ of the carotid bifurcation, and it is on the ground that epilepsy may be due to a disturbance /
disturbance of the cardio-aortic reflexes that he has advocated the extirpation of these bodies in this disease. The surgeons practising his operation remark in a work that the course of the disease was not appreciably influenced by the procedure. (34) This need arouse no surprise, considering how slender is the chain of 'evidence' on which the operation was devised.
SOME OBSERVATIONS ON THE HEART
DURING AND AFTER OPERATIONS FOR GOITRE.

In the course of the present research, opportunity has also been afforded me by Professor D.P.D. WILKIE of taking electrocardiograms of a number of goitre cases during the induction of anaesthesia, and throughout the course of the operation of thyroidectomy, while records have also been taken in several cases during the anxious first few days that follow the operation.

(a) In all, 10 cases have been followed during operation, and some of the results possess interesting features.

The first observation one would make is that the heart of the goitrous patient in its reaction to the anaesthetic and to the operation compares very favourably with the presumably healthy hearts of such cases as acute appendicitis or malignant cervical glands. One has been struck by the comparative rarity of disturbance of rhythm etc. arising during the anaesthesia and operation. Tachycardia, it is true, may be extreme, but similar high rates of over 150 have been recorded in a case of cholecystitis under anaesthesia, before the making of the skin incision. The initial tachycardia has usually been noted /
noted to increase during the induction of anaesthesia: in two cases a conspicuous bradycardia occurred (see below): but in general there has been little cardiac disturbance. This is possibly largely due to the choice of anaesthetic, a question which will be discussed later under that head. In all these cases, except for one performed under local anaesthesia, gas and oxygen has been used, with minimal quantities of ether: in all, preliminary scopolamine and morphine had been injected.

During the actual operation auricular fibrillation has never been noted to supervene: nor when initially present has it disappeared during the operation. In only five cases have noteworthy alterations in the cardiac action occurred, details being given below:

(i) Nodal rhythm. In a very severe case of Graves' disease, the resection having been completed, the surgeon was standing by demonstrating to the clinique the excised gland: the assistant had just finished catching bleeding points on the cut surface: and the patient for the moment was being interfered with in no way. The technician watching the string of the galvanometer noticed a sudden slowing of the heart; this recurred, and was recorded. There was no change in the patient's condition, which was quite satisfactory.
Fig. 35: - A.T., female, aet. 44 years.
Electrocardiogram, lead II, x ½ approx.
Nodal rhythm during operation.

Fig. 36: - M.D., female, aet. 52 years.
Electrocardiogram, lead II, x 1/3 approx.
Bradycardia during induction of anaesthesia with gas and oxygen.
The record (Fig. 35) shows an initial sinus rhythm at 150 per minute: after a few beats the "P"-wave (auricular) becomes inverted, denoting the activity of a new pace-maker in the auricle, probably near the a-v node: the rhythm slows to 100 per minute - 'Nodal rhythm' has become established. After four beats, "P" becomes upright again, and the sinus node regains control: the rate gradually increases again till the former rate of 150 per minute is reached, and maintained.

Nodal rhythm as we see it in medical wards occurs in slow beating hearts with over-active vagi, or where the sinus node has been damaged by toxins, etc. Why it should develop in a goitre with a tachycardia at 150, in the absence of operative interference with vagi or carotid sinuses, is not clear. The effect is possibly due to the anaesthetic: HEARD and STRAUSS report a case of nodal rhythm under ether anaesthesia, but they deny the influence of the ether. They suggest asphyxia as the cause, asphyxia being known to provoke nodal rhythm experimentally. No embarrassment of respiration was noted in the present case.

(ii) Bradycardia due to anaesthetic. In the case of a woman aged 52 years, with normal sinus rhythm, anaesthesia was induced as usual with gas and oxygen. Before /
Fig. 37: - B. MCM., female, aet. 18 years.
Electrocardiogram, lead II x 1/3 approx.
Bradycardia during induction of anaesthesia with gas and oxygen.

Fig. 38: - A.S., female, aet. 30 years.
Electrocardiogram, lead II x 1/2 approx.
Extrasystoles during course of operation.
Sinus arrhythmia was present before the induction, the heart rate was 105 per minute: with the induction it rose to 120 per minute. Two minutes later the rate was noticed to be much slowed, and a record was taken. Normal sinus mechanism persisted, but the heart rate was now 66 per minute, slightly irregular. During the operation the rate rose again to 80 per minute. Again, no clinical embarrassment was noted. A similar case is illustrated in figure 37. In this case, a girl of 18 years of age with marked thyrotoxic symptoms referable mainly to the heart was the subject. (Same case as in ergotamine charts on page 70). Her initial rate of 147 per minute drops during induction of anaesthesia with gas and oxygen to 93 per minute. Normal sinus rhythm is maintained. The effect was transient, and without subjective or objective appearances apart from the slowed pulse.

(iii) Bradycardia due to Carotid Sinus Reflex. One case showed a well marked transient slowing which could be definitely associated with a step in the operative technique. In the method adopted by Professor WILKIE the inferior thyroid arteries are caught, as a rule far out, and retraction of the common carotid is necessary for the display of the inferior /
LEISHMAN: Jas.

Records during operation.

Lead II: Part of record continuous with that shown below: before any dissection near inferior thyroid artery.

Lead II: Passing ligature round left inferior thyroid artery: knot tied at signal.

Lead II: Record at conclusion of operation.

Fig. 37a. J.L. Male, age 27 years.
Cardiac slowing due to stimulation of carotid sinus during thyroidectomy.
Gas and oxygen anaesthesia.
inferior thyroid artery and its successful ligature. Such retraction, it was thought, must of necessity pull on the sinus, and so stimulate the depressor reflex. SOLLMANN and BROWN (58) in 1912 had noted the bradycardia following on traction on the central end of a severed common carotid artery, an effect now attributed to HERING's reflex. As a routine therefore the ligature of these vessels was recorded in all cases. In one or two cases a very slight slowing was suspected: but in one case only did a definite bradycardia result. This was in a man, aged 27 years, where the passage of a ligature round the vessel caused the "R-R" interval to lengthen from 0.68 seconds to 0.86 seconds. (See Fig. 37).

(iv) Extrasystoles. These have occurred with no special frequency, but in one case a run of extrasystoles was noted to follow the application of a mass ligature or tourniquet to a lobe of the gland prior to the resection. The effect seems to have been asphyxial, from tracheal compression. It was not noted in other similar cases of application of this tourniquet. (Fig. 38)

One has been struck by the apparent slight importance of the carotid sinus reflexes in these operations: the ligature of the inferior thyroid arteries produced an effect only in the case noted above /
above: while the clamping or ligature of the upper pole has been followed in every case without revealing any effect on heart rate or rhythm. One's experience is certainly not in accord with the statement of HEYMANS\(^{31}\), that the excitability of these reflexes is an important factor to be watched during the operation. And HERING's advice as to preliminary cocainisation of the sinuses seems superfluous. A vagal slowing of the heart is not to be feared or deprecated in these cases, where sympathetic tone is so high, and where high rates are the rule. Nor is the blood pressure fall of such an order that it need cause anxiety .... the case reported by ENDERLEN and referred to on page 24 above seems exceptional, as that author later admitted.

(b) The post-operative courses of sub-total thyroidectomies have been the subject of much study of late years: those followed in the present research have yielded examples of what can be regarded as the typical varieties of these. Two examples will suffice: one of a rather stormy course with a regular rapid sinus rhythm, and the other of a fibrillating case yielding to normal rhythm some time after operation.

(a) Case /
Fig. 39. Charts of pulse-rate in post-operative crisis.

(a) A.T., female, age 44 years. Normal rhythm.
(b) M.McA., female, age 52 years. Auricular fibrillation.

The dosage of digitalis in each case is indicated: both cases received similar post-operative iodine treatment.

The height and duration of the tachycardia contrast markedly; and though case (b) was the more severe case it shows less reaction.
(a) Case with normal rhythm: A.T., female, aet. 44 years.

(b) Case with auricular fibrillation: M.Mca., female, aet. 52 years.

These were selected for consideration as cases of similar severity occurring in women of similar age and build, the only gross difference between them lying in the nature of the cardiac rhythm. One is in a position therefore to compare and contrast the post-operative course of the two cases so far as the cardiac condition was concerned.

In Fig. 39A is shown graphically the course of the pulse rate in the first case: one notes the rise from a pre-operative level of about 115 per minute to figures of 175-180 after the operation, and the persistence of the pulse at the 160 level for four days after the thyroidectomy, in spite of digitalis therapy. The pulse rate after the fourth day falls rapidly to more normal levels, and on the seventh day is under 100 per minute.

The electrocardiograms (Figs. 40, 41, 42) of this case show comparable features. There is marked tachycardia in all the records taken during the first four days, of which Fig. 40 is an example. There is then a gradual slowing of the rate (Fig. 41) till about a fortnight after operation it is as low as 75 per minute.
Fig. 40: - A.T., female, aet. 40 years. 
Electrocardiogram, leads I, II and III, 
day after operation.

Fig. 41: - Same case. 
Electrocardiogram, leads I, II and III, 
four days after operation.
Fig. 42: Same case.
Electrocardiogram, leads I, II and III, seventeen days after operation.
Apart from the changes in rate the electrocardiograms show little change of moment: there is no alteration in the rhythm, or in the conduction in the a-v bundle, etc. One notices a gradual increase in the amplitude of the deflections in lead III, but hesitates to offer any explanation. Similarly, the marked inversion of the T waves in all leads as seen in later records (Fig. 42) is a point whose significance lies open to debate. KRUMBHAAR in an early paper (Am. Jour. Med. Sci. Philad., 1918, CLV, ii, 175) considers "The development of diphasic or inverted T waves, especially in leads I and II, should probably be considered as influencing the prognosis unfavourably." This statement finds no confirmation from the course of this case: she made a satisfactory recovery. The inversion would probably be attributed by most English and American clinicians to a digitalis effect. Doubt has, however, been cast on the ability of digitalis to invert a previously positive T wave by the work of various German authors. This is a matter one can leave for the moment to the physician to decide: it is probably of more academic than practical interest to the goitre surgeon. The point of practical interest relevant to this thesis is that in spite of close observation and repeated records during the critical days that followed operation no disorder of /
Fig. 43: - M. McA., female, aet. 52. 
Electrocardiogram, leads I, II and III, 
day after operation.
(Auricular fibrillation).

Fig. 44: - Same case, twelve days later.
Electrocardiogram, leads I, II and III.
(Normal rhythm).
of the cardiac action was noted to occur, but that an extreme tachycardia persisted in spite of thorough digitalisation for the whole of the first four days.

In the second case, which is described in the ward records as "one of the worst cases operated on", the cardiac condition after operation was by contrast easily held in check. The case was one with auricular fibrillation, and as such one in which the ventricular rate could be controlled by digitalis with comparative ease. The post-operative pulse chart shows a maximum rate of 120 per minute; immediately before operation it was 160; at the conclusion of the operation it was only 110 per minute; six hours later it reached its maximum of (Fig. 39B) 120, and in two hours more had fallen to 94. It showed slight variations from hour to hour, but by the third day after operation was as low as 84 per minute, the fibrillation still persisting. The case was one which had had a preliminary ligation of vessels, and after this first operation she showed a transient return to normal rhythm. No such return occurred after the thyroidectomy till after her discharge to a medical ward, some twelve days later, (See Figs. 43 44), when spontaneous reversion to a physiological sinus rhythm occurred.

One would emphasise two points that are illustrated by /
by this case:—

(1) The comparative ease with which the heart can be controlled in a fibrillating as opposed to a non-fibrillating case. and

(2) The tendency to spontaneous reversion to normal rhythm even after many days from the date of operation.

These points have a bearing that will be further discussed under the heads of "digitalis" and "quinidine" therapy on pages 62 and 65.

(c) References to various cardiac complications that did not occur in the present series occur in the literature; of these one or two examples will be given.

RAFFLE, for example, makes the following statement in CHILE'S book on the thyroid gland:

"During the first few hours after thyroidectomy there may develop a bradycardia which may cause alarm if it is not understood. The pulse rate may become as low as 42 beats per minute. This condition is due to vagus stimulation and clears up in a few hours without special treatment."

The author makes no statement as to whether the cardiac mechanism in these cases remains normal, or whether heart-block is the cause of the slowing. No proof of the vagal aetiology of the condition is given by the author. From personal experience one can add nothing /
nothing to his statements, for no such case has as yet occurred under one's observation.

A somewhat similar case is described by Simon (57) where a condition clinically (but not electrocardiographically) diagnosed as heart-block occurred following the removal of a large cystic goitre (weighing 420 Gm.) from a woman of 50. After the operation the patient was very collapsed: her pulse imperceptible. On the third day after operation the heart was slow and irregular at 30 - 40 per minute. On auscultation, regular auricular sounds at normal rate could be heard, with slow and irregular ventricular contractions. The case was treated with atropin, calcium lactate, and digitalis - an odd association. The heart-block was attributed to vagal damage during the operation; and Simon says that such damage and consequent irritation is much more dangerous than actual division of the nerve.

Such an effect following thyroidectomy must be rare indeed, but in cases of malignant cervical glands the vagus is frequently deeply involved in the malignant mass. In one such case that came under personal observation, where the vagus had to be dissected clear of a mass of adherent glands, no change in heart rhythm or rate at the time or subsequently was detected. (Case III; series of Carotid sinus cases). The patient was in circuit with a string galvanometer throughout the operation.
(d) A word on the post-operative management of the heart in goitre cases may not be out of place here. One does not propose to discuss the use of sedatives, of general measures such as rest and proper temperature regulation, of glucose or of salines: the use of iodine, too, rests on such a firm basis of proven worth that it may be taken as a sine qua non of the post-operative routine. But one will discuss in a word the use of drugs directed specially toward the relief of the cardiac condition in these cases - digitalis, quinidine, and ergotamine.

One is of the opinion that the routine use of digitalis in these cases is to be deprecated. In this one has the support of HAMILTON who states that digitalis should be reserved for cases with irregular rhythm. In cases with auricular fibrillation and a rapid ventricular rate it is naturally of sterling value, and its worth cannot be overestimated. But in the commoner type of case, with a very rapid, regular sinus rhythm, it is of less efficacy. It is possible with digitalis to slow a sinus rhythm in children up to about 14 years of age, according to SUTHERLAND; but in the adult such slowing is exceptional. Even in the child this slowing cannot be elicited in the presence of fever or toxaemia: how then can one expect to attain it in the /
Figs. 45, 46, & 47: Electrocardiograms, lead II.

Mrs. P., aet. 32 years.
Case of digitalis over-dosage.

Top record shows partial heart block with dropped beats and two ventricular extrasystoles (coupled rhythm).

Middle record shows again dropped beats, and a ventricular extrasystole, followed by a run of similar ectopic beats.

Lower record shows paroxysm of ventricular tachycardia.
the adult, the victim of hyperthyroidism? When large doses are given, it is true, a slowing of the pulse may result, but this is usually due to the occurrence of an extrasystole after each normal beat, and the extrasystole being impalpable at the wrist may give the impression that the heart is beating at half the rate at which it actually is acting. Such a 'coupled rhythm' also only appears when the patient is on the verge of digitalis intoxication: and one of the features of this stage is the liability of the patient to sudden uncontrollable paroxysms of ventricular tachycardia. Electrocardiograms of such a case are shown (Figs. 45-47) they demonstrate partial heart block due to overdosage acting primarily on the bundle, with coupled rhythm due to extrasystoles, and finally a burst of extreme tachycardia of ventricular origin.

The case from which these records were taken was a woman whom one had the opportunity of seeing on the medical side of the hospital two years ago; she was aged 32 years, and suffered from exophthalmic goitre. In an endeavour to slow the pulse, digitalis had been pushed to the full, m.xx being given four-hourly for nine days. No sign of overdosage was evident till nausea appeared and the sudden development of dropped beats indicated the onset of heart block.
Fig. 48. Mrs. E. P., aet 32 years. Chart of pulse-rate to show comparative effects of digitalis and iodine in rapid, regular pulse of exophthalmic goitre.
classical electrocardiographic signs of grave digitalis poisoning were recorded - in fact, the rhythm changed from one form to another during the actual taking of the records. In the chart (Fig. 48) is drawn out a four-hourly record of the pulse rate during the period of digitalis administration, and during the succeeding period of iodine therapy. One notes that apart from two doubtful readings of 114 per minute on the 17th, the pulse rate was consistently high, from 140 - 156, till the 18th, when it started to fall steeply. It fell below 100 on the morning of the 19th; at the same time the patient complained of sickness, and it was clinically obvious that digitalis poisoning had set in. The electrocardiograms taken that afternoon, and referred to above, show the presence of partial heart block, of extrasystoles, and of paroxysms of ventricular tachycardia. On stopping the drug the symptoms rapidly improved. Lugol's Iodine was started, m.iii, t.i.d., on the 20th, and its effect on the pulse rate was obvious by the end of a week. On March 1st, for example, the pulse rate never reached 100 throughout the day. The point of chief interest from the present discussion is that no slowing of the pulse occurred until the stage of dangerous toxicity was /
Fig. 49: - Chart of digitalis action in children, after SUTHERLAND.

(Quart. Jour. Med. 1919, XII, 183)
was reached. The comparison is instructive between the pulse-chart of this case, and the chart reproduced from SUTHERLAND's paper (Fig. 49): in his series the average age of the patients was just over 7½ years, and all were rheumatic cases with rapid regular rhythm.

The use of quinidine for restoration of normal rhythm in cases of auricular fibrillation is now general, and in the fibrillation of goitre it has found considerable favour. The action of the drug is to prolong the refractory period, and the transmission times in the muscle, and so to break the circus movement which is the basis of auricular fibrillation. (EAST and BAIN, 19) Its use is not unattended with danger, however; in addition to mere intolerance (which may be manifested by headache, sickness, and diarrhoea) serious effects may follow its use. In some cases the fibrillating wave in the auricle is slowed so far that the ventricle responds to every beat, and the heart-rate leaps to a high figure. In other cases sudden death may follow from cerebral embolism, due to clots in the auricle being broken up and dislodged when normal auricular contraction is resumed.

Its use in goitre cases is not justifiable till the /
the toxic cause of the fibrillation has been removed -
that is, till after thyroidectomy. Once the operation
has been performed, persistent fibrillation is par
excellence the indication for the exhibition of the
drug. But it is not sound policy to give quinidine
too soon after the operation, for various reasons.
Its toxic effects, for example, should not be added
to the already heavy burden of the hyperthyroid
crisis; nor should it be employed till the rate of
the ventricle has been reduced to a moderate level
by digitalis. The chief reason for withholding the
drug is, however, that so many cases of auricular
fibrillation due to hyperthyroidism revert spontaneous-
ly to normal rhythm after operation. Such a
spontaneous reversion occurred for example in 48 per
cent. of DUNHILL's (18) series of 100 cases. The
change may not occur till many days after operation,
and one Edinburgh physician (Dr. EASON) has told
one that his practice is never to give quinidine till
a month after the operation. As by the end of that
period the usual case has left the surgeon's hands,
further elaboration of method of administration and
dosage are superfluous here. One may quote again
from DUNHILL the results of quinidine therapy in
these cases: in addition to the 48 per cent. who
reverted spontaneously in his series, 32 per cent.
returned to normal rhythm after quinidine. Only 7
per /
per cent. still fibrillated in spite of adequate operation and adequate treatment. (9 per cent. died after operation; 4 per cent. refused a second stage operation, being so much improved after a preliminary lobectomy).

One would sum up the drug from the surgeon's standpoint as one possessing powerful properties, but one whose use too soon after operation is neither justified nor safe. It is a drug for sparing use in after-treatment, not for post-operative management.

In the search for a drug that would influence the rapid sinus rhythm that is resistant to digitalis, various workers on the continent have for some years been using **ergotamine** in the pre- and post-operative treatment of goitre cases. As one has been able to do a certain amount of work with this drug of late, a short description of its properties and action may be fittingly appended.

Ergotamine, the active alkaloid of ergot of rye, is now procurable in a pure state (as ergotamine tartrate, known under the trade names of 'Femergen' in this country and 'Gynergen' on the continent; prepared by Sandoz). Constant potency of the preparation is thus assured: old galenical ergot preparations as used in midwifery practice were too unstable and erratic in action for general use. The action /
action of ergotamine as shown by DALE\textsuperscript{(11)} was to paralyse all motor fibres of the sympathetic nervous system: the inhibitory sympathetic fibres, he held, were immune. On this ground it was that DALE explained the reversal of the pressor effect of adrenalin injections by preliminary injection of ergotamine. More recently ROTHLIN\textsuperscript{(56)} has shown that the sympathetic inhibitory fibres are also paralysed by the drug, while mild vagal stimulation may also occur.

The application of the drug to goitre therapy lies in the supposition that tachycardia is the result of excessive sympathetic stimulation in this disease. It is a moot point whether thyroxin has also an action directly on the heart: some workers are of opinion that it has; but ENDERLEN and BOHNENKAMP\textsuperscript{(21)} found from animal experiments that thyroxin has little or no effect on the hearts of dogs after extirpation of the stellate ganglia. We can take it therefore that by paralysis of the accelerator fibres the flogging action of thyroxin on the heart would be largely avoided. Whether ergotamine can or can not secure this sympathetic paralysis is not definitely settled; HENRIJEAN and WAUCOMONT\textsuperscript{(27)} seem to doubt it, but the balance of evidence is in favour of ergot possessing this power, as for example the paper by ANDRUS and MARTIN /
MARTIN(3), who found that following the functional exclusion of the vagus, ergotamine produced slowing of the sinus rhythm, as well as other effects on conduction, etc. attributable to sympathetic paralysis.

Reports on the clinical use of ergotamine in goitre cases have been published by ADLERBERG and PORGES(1), JAGIC(35), MERKE(45)(46), MERKE and BISNER(47), NOYONS and BOUCKHAERT(50), ROTHLIN(55),(56), and STAHELIN(59). The dosage employed is small: from $\frac{1}{4}$ - $\frac{1}{2}$ milligramme suffices for a dose given by intramuscular or subcutaneous injection, or $\frac{2}{3}$ milligramme per os. There is some individual variation in tolerance, and unpleasant reactions may follow even small doses. These usually take the form of nausea and vomiting, but praecordial discomfort may be a feature, as is noted by JAGIC(35), who saw 'repeatedly acute heart disturbances occur, probably due to the sudden onset of peripheral hypertension.' Such a reaction occurred in one case personally treated, where the dose employed was only 0.125 mg. intramuscularly: this patient tolerated the same dose next day without any reaction, and later bore doses up to $\frac{3}{4}$ mg. by injection without much disturbance. (See charts appended). The most serious complication is one which does not follow a single dose, but may supervene during the course of repeated administration: this /

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* This work was done in collaboration with Dr. J.D.S. Cameron, F.R.C.P., to whom I am indebted for readings of pulse and blood pressure.
Graph to show effect of Ergotamine on pulse rate and diastolic blood pressure.

The systolic blood pressure showed relatively little rise, being 135 mm. Hg. before injection, reaching a maximum of 144 at noon, and falling back to 136 at 12:45 p.m.

**Effect of Ergotamine on Pulse and B.P.**

(1 mg. tartrate, intramuscularly at arrow)
this is peripheral gangrene, affecting usually the toes, and necessitating in some cases amputation. A typical case of this sort is reported by MERK£ (46) where the gangrene came on after ergotamine had been given $\frac{1}{2}$ mg. b.i.d. for seven days, and then 1 mg. b.i.d. for two further days.

So much for the unpleasant side-effects: on the other hand ergotamine seems to have some therapeutic value in these cases. It produces a slowing of the pulse, a rise in diastolic blood pressure, and a fall in Basal Metabolic Rate (NOYONS and BOUCKHART (50))

These effects are detectable after a single injection, and are said to become more marked after a course of ergotamine therapy. It must be emphasised that the effect of a single injection is very short-lived. In the case on which one tried the drug personally, the pulse slowing and rise in blood pressure had disappeared in a matter of two and a half hours after each injection.

The charts and electrocardiograms appended (Figs. 50, 53) are from this case of toxic goitre in a girl of 18 years, and show the typical slowing of the pulse, the rise in diastolic pressure, and the transient nature of the effects. Notes are made on the chart as to the subjective phenomena experienced by the patient.

Even the advocates of the drug emphasise that it is /
Fig. 51: Record at 12 noon; Fig. 52: Record at 1.35 p.m.

Note slowing of heart in second record, without change in form or duration of complexes; and note transitory nature of the action.

B. M. M., female, aged 18 years. Ergotamine test.
Electrocardiograms, leads I, II and III in each.
Ergotamine tartrate, 0.187 milligrams at 11:45 a.m.
Fig. 52: Record at 4:55 p.m.
is in no sense a 'curative agent': it relieves the symptoms and the heart condition, but does not remove the underlying cause of the disturbance. On stopping the drug the tachycardia etc. return in a short time. This one may correlate with the findings of VOLKMANN (63) who in his paper on the treatment of goitre with Lugol's iodine compares the striking differences in the results of iodine and of ergotamine therapy on the histological picture of the gland. The colloid change due to iodine is associated with the more direct action on the gland: ergotamine has quite another point of action.

The value of ergotamine, one would say, lies in having a drug at hand which will slow the heart in those cases resistant to digitalis and iodides. In view of the individual variation in tolerance, a preliminary test before operation to determine the optimum dose would be an advantage when the crisis arose demanding its immediate use. Severe ergotism in the form of gangrene need not be feared when the drug is employed only as an occasional emergency measure: it is a real danger with prolonged use.
The heart under anaesthesia:

With special reference to operations on the neck.

There are abundant references in the literature to the action of the various anaesthetics on the hearts of experimental animals, but details of the action in man are curiously lacking. Such analyses of the cardiac action as have been carried out are embodied in the following papers.

In 1912 Ritchie\(^{(53)}\) published a case of cardiac disturbance arising in a young man of 19 during the course of chloroform anaesthesia, which was analysed by polygraph, and found to be an auricular flutter, with an auricular rate of 454 per minute, the ventricular rate being about 190 and irregular. The disturbance appeared after anaesthesia had been in progress for 30 minutes; it persisted for three minutes, when the patient became cyanosed, and the anaesthetic was stopped; artificial respiration was applied, and after one minute the pulse, which had been alternating and rhythmic, became wholly irregular - auricular fibrillation had developed. Two minutes later the ventricles and auricles had resumed their rhythmic action at 125 per minute: the irregularity did not recur.

Heard and Strauss in 1918\(^{(26)}\) in a report on two /
two cases of nodal rhythm studied electrocardiographically, give details of a case in which the condition developed for the first and only time in a woman when under the influence of ether anaesthesia. They mention that twenty-one other cases were studied by the electrocardiograph under ether without this abnormality being detected in any, and discount the influence of the ether in its production. The pre-operative dose of morphine is likewise discounted. The small routine dose of atropin before operation they consider may have played a role, it being known that carotio-vagal pressure a short time after a dose of atropin may produce nodal rhythm. They also discuss the part asphyxia may play in its production.

The only reference to the electrocardiographic recording of the heart-action in man during chloroform anaesthesia that one has found is by GLUZET and TIXIER⁹, working in Lyons in 1919. Six of their eleven cases were under chloroform. All showed marked slowing of the heart, even to half its original rate. They found no modification of the three principal waves of the electrocardiogram, except a little diminution in amplitude. In two cases they noted frequent extrasystoles, negative in lead II. Five cases under ether showed no abnormalities whatever. They noted marked electrocardiographic changes associated /
associated with operative procedures involving shock - evisceration, dilatation of the anal sphincter, etc. In these cases tachycardia, auricular fibrillation, and frequent extrasystoles occurred. One sentence from their summary must be quoted in full, in view of one's personal somewhat contradictory experiences.

'En résumé, l'anaesthésie générale au chloroforme produit pendant la résolution musculaire un ralentissement du coeur et quelquefois des extrasystoles, mais non les troubles électrocardiographiques considérables observés chez le chien.'

(These disturbances in the dog are described by CLUZET and PETZETAKIS[8] as of the nature of heart block, approaching Stokes-Adams attacks)

In 1920 LEVINE[39] described nine cases showing acute cardiac disturbances following surgical operations, seven of them under a general anaesthetic (ether). These disturbances were:-

in three cases, paroxysmal auricular tachycardia:

in four, paroxysmal auricular fibrillation;

in two, paroxysmal auricular flutter.

The most important paper on the effect of anaesthetics on the human heart is that by LENNOX, GRAVES, and LEVINE[38], in 1922. In their series of fifty patients, all electrocardiographically observed, twenty had ether anaesthesia, twenty-two had gas and oxygen, and the other eight had local anaesthesia. /
anaesthesia. No case in their series had chloroform. In about half of their cases some abnormal mechanism was present under the anaesthetic, not present before induction. The usual forms were paroxysmal auricular tachycardia, premature beats, and marked displacement of the cardiac pacemaker. They found that disturbances of all kinds were most frequent in operations on the head and neck .... 70 per cent. of these showed some abnormality, while 40 per cent. of the remainder only were abnormal. Again, disturbance of the pacemaker was present in 46 per cent. of operations above the clavicles, but in only 13 per cent. of operations elsewhere. 'In several instances abnormality seemed to follow critical steps in the operative procedure, but in the great majority of cases no such relationship was evident.' The authors suggest that vagal stimulation is in some way concerned in the production of the abnormalities.

As an incidental part of the investigations reported in this paper a number of observations have been made on the action of anaesthetics on the human electrocardiogram. These have been carried out not only throughout the course of various surgical operations, but in the stage of induction of anaesthesia /
D.McG., male, aet. 66 years.

Case V of Carotid Sinus series.
Electrocardiograms, lead II x 3/7 approx.

Showing effect of chloroform on the heart's action during induction of anaesthesia.
anaesthesia, in which in fact most of the interesting developments have occurred.

Some twenty anaesthetics have been followed in nineteen cases: in ten cases the anaesthetic was chloroform for induction, followed in some by ether, in others by gas and oxygen, while in two cases chloroform was used throughout. In eight cases gas and oxygen was used for induction, and in two ethyl chloride followed by ether.

Chloroform. In several cases striking disorders of rhythm have resulted from the use of chloroform: examples of these are shown in figures 54 to 58. In each case the disordered action started during the period of induction, and had practically disappeared before the third stage of anaesthesia was reached. In each case too, the nature of the disorder was the same: a period of simple tachycardia was followed by one where numerous extrasystoles were recorded, arising from both ventricles, a veritable 'anarchie du coeur'. This is seen in its most extreme form in Fig. 55, while less severe forms of coupled rhythm are seen in Figs. 56, 57, 58. Similar appearances of coupled rhythm due to ventricular extrasystoles is seen in Figs. 25, from Case I of the carotid sinus series, where the disorder was provoked by vagal pressure, by stimulation of the sinu, and by stimulation /
stimulation of the vagus nerve directly in a patient under chloroform anaesthesia. (See page 34).

These disturbances are much more serious than one would gather from the paper of Cluzet and Tixier; and they show a striking similarity to the tracings obtained from the cat under low percentages of chloroform vapour by Levy and Lewis. In a subsequent paper in which the relationship of the extrasystolic irregularity to the fatal ventricular fibrillation that follows in the cat on any slight stimulation while in this state (e.g. by injection of small doses of adrenaline, nicotine, etc.) Levy states:

'It is possible to make the important statement that in every single instance of ventricular fibrillation induced under chloroform by any of the methods I have employed, it has been preceded by a stage of complex ventricular irregularities, so that unquestionably the one condition leads on to the other, whatever their relationship may be.'

Levy looks upon chloroform death in man as due to ventricular fibrillation: he states that in animals a stage of complex ventricular irregularity is present before the onset of fibrillation. The demonstration of this stage in man so far as one is aware has not before been published. In a recent paper, for example, Parade states "Although the certain electrocardiographic evidence from man is lacking, that /
Fig. 57:— J.K., male, aet. 63 years.
Case IV of Carotid Sinus series.
Electrocardiogram, lead II x 3/7 approx.
Record taken seven minutes after induction of anaesthesia with chloroform.

Fig. 58:— A.S., male, aet. 62 years.
Case VII of Carotid Sinus series.
Electrocardiogram, lead III x 3/7 approx.
Record showing effect of chloroform on the heart's action during induction of anaesthesia.
that with chloroform death ventricular fibrillation is involved, the conclusion is hardly to be doubted". One may put forward the tracing in Fig. 55 as a step forward on the way to the demonstration of the condition in man.

In the taking of these records particular attention has been paid to the passage of the intratracheal catheter: in Fig. 58 the signal denotes an attempt to introduce the tube through the larynx. It seems that vagal stimulation is very likely to result from interference with the cords, and one is curious to know how far such stimulation modifies the electrocardiogram. It is possible that a premature attempt to introduce the tube during the early stage of anaesthesia with ventricular hyperexcitability might provoke very serious results.

It is noteworthy that in all these cases where cardiac disturbance was manifest electrocardiographically the anaesthetist was quite unaware of the disorder, and complacently continued his administration. In the increased dosage of chloroform that results from this continued administration lies probably the reason why fatal results are not more frequent. LEVY has shown that the disorders produced in cats by low concentrations of vapour are not produced with higher concentrations, and are in fact abolished by higher /
higher percentages. He states that this is due to dilatation of the ventricles under the higher concentration of the drug, resulting in lowered intraventricular tension and diminished liability to fibrillation or extrasystole-formation. It is also to be noted from the present series of records that such irregularities as have been recorded all occurred during the early stages of the anaesthesia, and disappeared before the full surgical stage of anaesthesia was reached: this is in accord with animal experimental work.

Such emphasis has been laid on these cases showing disorders of cardiac action during the administration of chloroform that one is in danger of giving the impression that such disturbances are the rule with this anaesthetic. This is not the case: they occurred in only three of nine cases examined: in one patient who was twice anaesthetised, extrasystoles were much less numerous on the second occasion than on the first. There appears to be a big individual variation in susceptibility, and even a variation in the same person from time to time: but though for some people chloroform may be a relatively safe anaesthetic, the occurrence of grave disorders in 30 per cent. of cases observed is sufficient argument against its promiscuous use. The precise
mechanical methods of the electrocardiograph have in this case served to bear out the clinical conviction born of experience, that chloroform is an unsafe drug.

**Gas and Oxygen.** In eight cases where anaesthesia was induced by gas and oxygen and followed electrocardiographically one has never seen any disturbance comparable to those seen under CHCl₃. Abnormalities in the records do occur, however: reference to these has already been made in the section on Goitre (q.v. page 53). Bradycardia during induction occurred twice, and was marked. The P-waves were noted to disappear with induction on several occasions. And in one case under gas and oxygen nodal rhythm was noted for a few moments at the conclusion of the operation (see p. 52).

**Ethyl Chloride.** In the two cases where induction was observed by this drug, no grave effects were noted. The P-waves were again noted to disappear with induction; it will be noted that this disappearance of P-waves occurred with all the anaesthetics, including chloroform (see Case I, carotid sinus series).

**Importance of anaesthetic relative to neck operations.** From the findings of LENNOX, GRAVES, and LEVINE (38) regarding the frequency of cardiac disturbances during operations above the clavicles, one /
one may judge that the influence of the anaesthetic has more than an academic interest. From the records personally made during chloroform induction, one may conclude that chloroform is at all costs to be avoided for operations where any interference with the vagi is likely to occur, either directly or reflexly. It is a bad precursor of the introduction of an intratracheal catheter for this reason, and an equally bad forerunner of operations involving dissection round the vagus trunk or carotid sinus. The exaggeration of the carotid sinus reflexes under chloroform is referred to by ROSKAM in his paper advocating preliminary estimation of the reflex in cases about to undergo operations upon the antero-lateral region of the neck. Gas and oxygen seems to be as nearly ideal as may be, and its claim on clinical grounds to be the safest anaesthetic is confirmed by electrocardiographic study.
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