THESIS

THE PHYSIOLOGICAL BASIS OF NEUROCIRCULATORY ASTHENIA

by

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I. INTRODUCTION

1. History.

McLean's description of the syndrome in 1864, is possibly one of the first attempts to correlate active military life with Neurocirculatory Asthenia (117). He believed that the disease was limited to soldiers and that a definite pathological change in the heart occurred in this syndrome. The following excerpts from McLean's article epitomizes his views on the subject.

"And, first are diseases of the heart and great vessels more prevalent in the army than in civil life? I think so."

McLean's description of a heart, typical of Neuro-circulatory Asthenia is suggestive that his pathological exhibits were those of organic heart disease - possibly coronary artery disease.

"Again, I have often pointed out to you that nothing is more common, than to see cases here of well marked hypertrophy of the heart without vascular disease. The obstacle is not at the outlet of the heart's chambers; it is one which interferes with the free and healthy play of the organ. Look at this preparation. Mark this remarkable white spot on the external surface of the heart. It is as large, you see, as a five shilling piece. What is it? Nothing, apparently but a substance analogous to a corn; as much the result of friction and undue pressure, as are the torturing corns with which we are afflicted by unskillful bootmakers. We call it here "the soldier's spot", so common is it on the hearts of soldiers at our post-mortem examination."

McLean gave the name "irritable heart", to this condition. This fact is not generally known and La Costa is usually given credit for the term "irritable heart". This name is now supplanted by the name Neurocirculatory Asthenia. McLean states "the official nomenclature in use in the service has no heading under which to include what maybe called "irritable heart"--that rapid, often tumultuous action so common among soldiers."

McLean was adamant in his views that irritable heart was due to the great amount of equipment a soldier was required to carry in battle. He stated that if soldiers were freed from this encumbrance the disease would not be seen in future generations.

McLean's work, though possibly the earliest, is not necessarily the best of the earlier work. The syndrome was described in soldiers who fought during the American Civil War by Hartshorne in 1867 (73) and Da Costa in 1871 (39). Of the two Da Costa's work is by far the more outstanding. His views and conclusions concerning "irritable heart" were based upon his study of 300 cases of the condition. These views were far reaching and are tenable to a great extent to-day. The following passage taken from his article supports the above contentions.

"In this paper I propose to consider a form of cardiac malady common among soldiers, but the study of which is equally interesting to the civil practitioner, on account of its intimate bearing on some obscure or doubtful points of pathology. Much of what I am about to say I could duplicate from the experience of private practice; (opposed to McLean's views) yet, I prefer to let this enquiry remain as it was originally conducted on soldiers during our late war."

demonstrable pathological changes thereof. In the twelfth edition of Osler's Medicine by McRae, the author was convinced that "functional heart disease was a definite clinical entity without any pathological changes to account for the symptoms". It remained for Lewis, however, to observe that functional heart disease and "effort syndrome" (irritable heart) were of the same nature.

Oppenheimer and Rothschild, working in collaboration with Lewis during World War I, suggested that the name Neurocirculatory Asthenia be used for the syndrome. They believed that constitutional defects were the greatest single cause of Neurocirculatory Asthenia. These individuals were, in their opinion, a constitutionally inferior group who were more prone than normal individuals to develop abnormal behaviorisms in times of stress. Neurocirculatory Asthenia in their opinion is just an abnormal behavior pattern (130).

Oppenheimer's and Rothschild's views are possibly the most modern and have been upheld by men such as Caughey (29), Wood (178) and Weiss and English (162). The latter two men have stated in their text book of psychosomatic medicine that Neurocirculatory Asthenia is not a disease of the heart, but "the disorder is always of the total personality".

There have been numerous contributions to the literature concerning Neurocirculatory Asthenia. Most of these, in my opinion, have only brought out a new hypothesis concerning the disease which has later been disproven (2, 7, 12). Some men have merely described tests of questionable nature (20, 88) which others fail to confirm (180), while a few men reviewed the literature and gave support to the modern psychosomatic view of the syndrome (29, 65).

Thus, McLean's original concept that the syndrome is due to organic heart disease with demonstrable pathological changes has evolved into an entirely different concept. Specialists in psychosomatic medicine categorize Neurocirculatory Asthenia as a disorder of the whole personality without any evident pathological heart disease.

2. Definition of Neurocirculatory Asthenia.

Neurocirculatory Asthenia is a syndrome which has been described on innumerable occasions (160). This in itself indicates that unanimity was lacking with regards to its etiology or understanding of its symptoms. In studying the pathologico-physiological basis of the syndrome, it may be well to mention first some of its more popular designations as follows:

1. Da Costa's Syndrome (Wood)
2. The Irritable Heart (McLean and Da Costa)
3. Effort Syndrome (Lewis)
4. Muscular Exhaustion of the Heart (Hartshorne)
5. X-Disease (MacKenzie)
6. Cardiovascular Neurosis (Caughey)
7. Orthostatic Tachycardia (Bass and Wessler)
8. Vasoneurosis (especially of children)
9. Soldier's Heart (Lewis)
10. Autonomic Imbalance (Kessel and Hyman)
11. Disordered Action of the Heart (D.A.H. of the British Army)
12. Neurocirculatory Asthenia (Oppenheimer and Rothschild)

The designation of the syndrome in this thesis as "Neurocirculatory Asthenia" is preferred for the following reasons:

1. The syndrome manifests itself in stresses other than pure physical effort.

2. The syndrome has a strong psychological element and the patient evidences fear of a damaged cardiovascular system.

3. The name does not imply that the syndrome is limited to individuals in the armed forces.

Neurocirculatory Asthenia is a state of ill health characterized by a group of symptoms consisting of dyspnoea, effort trouble, palpitations, precordial pain, exhaustion, dizziness, nervousness and sometimes tremor, perspiration, headache and syncope. These symptoms are all aggravated by effort or excitement. The syndrome is prevalent in individuals who are hypersensitive to emotional and physical stresses.

3. Case History.

The following is a case history of Neurocirculatory Asthenia which illustrates most of the features of the syndrome. This history was taken from the files of the Royal Victoria Hospital.

Cpl. T.D., R.V.H. No. 43-7849 Age 28.

Complaints: 1. Dyspnoea and palpitation on moderate exertion.
2. Occasional headaches and dizziness.
3. Occasional precordial pain.
4. Occasional sore throats.
5. Three fainting attacks in last three years.

Family: Mother - 52, alive, is very nervous and has been in poor health for at least five (5) years. He states that she has now had heart trouble for two (2) years,

but he does not know what kind.
Father - 52, alive, has been troubled with stomach trouble of unknown kind for four (4) years.
Three (3) sisters - two are A. & W. One aged 33, has been an invalid since some illness at the age of 7.
One (1) brother, A. & W.

Personal: The patient was born in Montreal, and has lived there until joining the army a little over two (2) years ago. Before joining the army he worked for the City of Verdun, working a pneumatic drill. He was married in 1934 and they now have four (4) children, three (3) boys, 8, 7, and 6, and one (1) girl aged 4.
They are all well. His wife has been very nervous for the last seven (7) years, finding it too much work looking after the four (4) children. He has his own home and his wife gets $99,00 per month dependents allowance on which she manages to keep the home reasonably well.

Functional. Eyes - Vision is normal. Does not wear glasses. States he has occasional diplopia.
Ears - Hearing normal. No ringing or buzzing. Occasional dizziness on standing.
Head - Has had numerous headaches during the last three (3) years, since receiving a blow on the head, at which time he had 15 stitches at the Montreal General Hospital. The headaches are mainly frontal, although some pain in the left temporal region where

he received the blow. Since that time he has fainted three times, twice in civil life, both times while walking around the house and once in the army when walking into a theatre. He had not been drinking on any of these occasions.

Nose an throat - Before joining the army he had about 6-7 sore throats a year and only about 1 per year since. He has 4-5 colds a year. He has no trouble breathing through his nose, and no post nasal discharge.

Respiratory - No complaints.

Cardiac - Palpitation and dyspnoea on moderate exertion for the last nine (9) years, also crampy pains in his stomach region with exertion. With the palpitation he is conscious of his heart pounding in his chest.

Alimentary - He states that he has a poor appetite, but that there are no foods he does not eat. He rarely has indigestion. Bowels are regular, moving every 2-3 days. He occasionally takes castor oil. He says he takes alcohol poorly, becoming quite drunk on four (4) quarts of beer in three (3) hours. He has a bad hangover the next morning.

G.U. - No nocturia, dysuria, etc. Denies V.D.

Locomotor - He has occasional rheumatic pains in the right shoulder and left knee, particularly during the winter. He has never had rheumatic fever.

Integumentary - He has suffered from ache on his back.

Nervous system - Often breaks into a sweat p.c., particularly after lunch. Twice a day he has sudden feelings of heat and sweating, which may occur even while at rest.

His hands are usually cold and clammy. He sweats excessively particularly in hot weather, but prefers hot weather to cold.

Present Illness: This apparently healthy soldier was returned from overseas as an instructor. He has not complained, but on routine examination he was noted to have a rapid pulse, at first of 150, and never below 120-130. He has had four (4) weeks of leave since returning home without any apparent improvement. He states that he has had trouble with his heart for the past nine (9) years. The first symptoms he remembers were a consciousness of a rapid pulse, and a feeling that his heart was trying to stop. At these times, his breathing was difficult and he had a tight feeling around his chest, and was breathing rapidly. He was only occasionally conscious of these symptoms. Six (6) years ago he was sick in bed for three (3) weeks at home, apparently with tonsillitis, and he thinks with heart trouble too, although he doesn't know.

He doesn't believe that he has had any heart trouble since joining the army 2-3 years ago. While in England he took a Commando course lasting 24 days. He found this very difficult, particularly the running, because of palpitation and dyspnoea. He always managed to get around the course but usually finished about 20-25 minutes behind the rest of his class.

He was nervous during air raids, and particularly nervous during manoevers on which live ammunition

was used.

He says he likes the army and would like to remain in it.

Physical: Patient is a well developed and well nourished young white male appearing to be about stated age of 28.

Weight - 162 lbs., height - 5'7¼".

He does not appear to be ill or nervous.

Head - Normal size and shape. There is a small scar in the left temporal region.

Eyes - Pupils react to l & a. Slight nystagmus, no strabismus. Fundi appear normal.

Ears - Considerable wax in canals. Drums appear normal.

Nose - Muco pus in right nostril.

Mouth - Tongue protrudes in midline without tremor, moist, slightly coated. Tonsils are of large buried type, hypertrophied and inflammed. Teeth need cleaning. They are in good condition except for lower 2nd molar, which has a corner knocked off.

Thyroid and cervical glands - Not enlarged.

Chest - Chest is large and well developed and moved with respiration. PN clear through. BS normal. No adventitious sounds.

Cardiovascular - Heart is not enlarged to percussion. Heart sounds are normal. The pulse was 120 at the beginning of the examination, and fell to 80 later on, and then rose again immediately to 104 when the patient sat up. B.P. 130/84.

Abdomen - The abdomen is muscular, no scars, no masses or enlarged organs palpated. No deep tenderness.

G.U. Negative. Locomotor - negative.

Integumentary - Acne vulgaris on back.

Nervous - Reflexes physiological. Normal response to touch and vibration.

Special Examinations:

Haemogram June 25th/43. R.B.C. 5,400,00 W.B.C. 9,400
Sed. rate 18mm. 1st hour
25mm. 2nd hour.

O.T.L. June 10/43. Recommend - 1. X-Ray of Sinuses
2. Tonsillectomy later.
Diagnosis: Chronic septic tonsillitis.
Dr. K. Hutchison.

X-Ray June 10/43. The cardiac and aortic shadows are not unusual. Both lung fields are clear. Conclusion: Healthy chest.

X-Ray June 10/43. Frontal, anterior ethmoids, and left maxillary sinus show no gross evidence of disease.

In the inferior view of the right maxillary sinus, there is an increased density with a rounded upper border suggestive of muco-periosteal hyperplastic disease or polyp formation.

Dr. H. Brooke.

E.C.G. June 8/43. Rate 72, regular. Left axis deviation. The QRS complexes are slightly slurred, and there is a slight tendency to an elevation of the R-T interval in lead one. There are some coronary artery changes -

probably an early sclerosis.

Dr. C.F.Moffatt;

June 13/43 Rate 96, regular. Fourth lead is normal. Left axis shift. Conduction time normal. The slight elevation of the R-T interval previously noted has now practically disappeared. The tracing falls well within normal limits.

Dr. C.F. Moffatt.

B.M.R. June 10/43. The present electrographic examination was completely negative, even during hyperventilation. This would argue against an epileptoid basis for the "fainting spells".
Greater certainty would be possible if one could obtain an electrogram during one of his spells.

Dr. H.H. Jasper.

Psychiatry: This man gives the usual past history given by soldiers who have developed neurosis under slight strain. As a child he was afraid of the dark and his mother kept a light in his room. He had enuresis until the age of 12. He has bitten his finger nails off and on, up to the present, although they give no evidence of being bitten right now. He has had slight stuttering under nervous stress and he had a nervous blinking of his eyes at age 16 or 17.
As a boy he avoided fights. He has always been a restless sleeper and if faced with an exciting event he would be unable to get to sleep for hours and he

would be off his food for two or three meals.
He has also had headaches and dizziness off and on since the age of 16 or 17. He entered the army because several of his friends had joined, and after three months preliminary training was sent to England. He had palpitation, nervousness, headaches, and dizziness off and on but continued to carry on. During Commando training in which they used live ammunition, he felt very apprehensive, but he kept it for himself and never let on to his associates. He was sent back to Canada as an instructor and then given two weeks embarkation leave before returning to England. Following this, a medical board discovered his rapid pulse although he was making no complaint of his symptoms which he had had. His wife is not well and two of his children have suffered accidents.
Rorschach examination reveals very marked color shock and shading shock with failure to interpret several of the cards. This is consistent with a markedly neurotic personality.
The Rorschach record, which reflects merely the personality at the time of the examination, could be rendered more neurotic by a somatic influence, such as a focus of infection as throat or sinuses, but the past history gives strong evidence of his always having been of a "nervous constitution". This is assuming that he has not learned all the appropriate answers to the personality questionaire and it is my impression that he is telling the truth.

Dr. W. D. Ross.

Histamine Curve July 3/43:

Blood control---------- 7.0 gamma/100 cc. blood.
5 min. after injection-- 4.5 " " " "
15 " " " -- 4.5 " " " "
30 " " " -- 5.0 " " " "

A severe headache started 3 minutes after the histamine injection lasting for 25 minutes. The blood pressure dropped from 130/70 to 115/70, the pulse also became slower, the pulse feeling very weak and thin. The eyes became bloodshot.

Dr. Wolfe.

Cardiovascular Stability Tests:

	June 15	June 17	July 16
Schneider	-1	-1	-5

	June 18	June 23	July 6	July 20	July 26
Harvard	18	33	29	29	40

	July		
Cold Pressor	Increase systolic 16		Increase diastolic 6

II. THEORIES OF ETIOLOGY

1. Occupation.

The contention that civilian occupations have no bearing on the prevalence of Neurocirculatory Asthenia in the Army (38) is now considered antiquated (103, 130, 131, 178). The table to follow shows that civilian occupations do play their role in Neurocirculatory Asthenia. Patients with Neurocirculatory Asthenia have a predilection for sedentary work. Whether they are physically unfit for hard physical work or whether they

naturally shun hard physical work is still unanswered.

Patients with Neurocirculatory Asthenia

	Simple Tasks	Light Duty	Hard Labour
Oppenheimer & Rothschild (130, 131)	80.4%		
Wood (178)	53%		
Lewis (103)	57%	20%	23%

It will be noted that in these series the majority of individuals performing "simple tasks" suffer from Neurocirculatory Asthenia.

2. Sex.

It is a misconception that Neurocirculatory Asthenia is more prevalent in men than in women. This is true only in wartime. In civilian life women suffer to a much greater extent than men, to wit: 58.6% to 41.4% (167) and 69% to 31% (83).

3. Age.

Combatant soldiers have no monopoly on Neurocirculatory Asthenia. It is found in civilians from early childhood (13, 98) to middle age (38, 55, 85). Frail and sickly children are more likely to develop Neurocirculatory Asthenia, than is the healthy youngster (13).

Craig and White state that in civilian life the average age of onset of Neurocirculatory Asthenia is 31.5 years (36) with extremes ranging from twelve to sixty-nine years. Neurocirculatory Asthenia in soldiers occurs most frequently between the ages of twenty and thirty. The following table is the author's summary of results compiled by several investigators.

The first column is taken from White and Jones (167) and illustrates the percentage distribution of Neurocirculatory Asthenia in civilians of various ages.

The second, third and fourth columns were taken from da Costa (39), Friedlander and Freyhof (55) and Hume (85) respectively. These latter columns illustrate the percentage distribution of Neurocirculatory Asthenia in soldiers of various ages.

The fifth column is the average of the second, third and fourth columns. This average was calculated by the author to strengthen the contention that Neurocirculatory Asthenia in soldiers occurs most frequently between the ages of twenty and thirty. The average must be taken with reservation as most soldiers fall into this age group (103).

Age	(167) %	(39) %	(55) %	(85) %	Average %
0-15 years	0	0	0	0	0
15-20 "	15.3	25.0	2.0	7.9	11.6
20-30 "	7.4	60.0	86.0	56.4	67.0
30-40 "	23.9	8.5	12.0	24.7	15.0
40-50 "	27.4	6.5		11.0	8.7

4. Pressure from Clothing.

"The soldier has to make the severest exertion at the utmost possible disadvantage, as regards the weight he has to carry, the mode in which he has to carry it and the entire arrangement of this dress and equipment" --- "the soldier is strapped around the waist and can't breathe fully" (117). Clothing adjustments should be made "to allow no pressure on the muscles, nerves, arteries, or veins". These now obsolete

theories were postulated by McLean (117) and Meyers (129).

5. Tobacco.

Tobacco cannot be considered as a cause of Neurocirculatory Asthenia for neither has it been proven to be detrimental to those suffering from Neurocirculatory Asthenia, nor has it been found that these individuals smoke more than normals (103).

Parkinson and Koeford (133) found no remarkable difference in comparing the effects of smoking on normal individuals and on those suffering from Neurocirculatory Asthenia.

Their table, which follows below, illustrates the above contentions.

(After smoking 20 cigarettes)	Neurocirculatory Asthenia	Controls
Increase of pulse rate	9	6
Rise of systolic B.P.	7 mm.Hg.	6 mm.Hg.
Rise of diastole B.P.	5 mm.Hg.	5 mm.Hg.

In a series compiled in this laboratory and that of Aronovitch (127), which together comprised thirty cases, there was a negligible degree of correlation between smoking and Neurocirculatory Asthenia (7, 133). The following table is Lewis' summary (103) which may be taken as the general consensus of opinion. The table indicates that cigarette smoking is not more prevalent in patients with Neurocirculatory Asthenia.

	Neurocirculatory Asthenia 461 cases	Heart Disease 87 cases	Gun Shot Wounds 100 cases
Non smokers	6%	13%	2%
2 cigarettes daily (one ounce a week)	20%	22%	3%
5 cigarettes daily	42%	40%	23%
10 cigarettes daily	27%	22%	49%
20 cigarettes daily	4%	1%	21%
25 cigarettes daily	1%	2%	2%

6. Infections.

The concept that infection plays an important part in the production of Neurocirculatory Asthenia dates back to Da Costa's time. Since then, this concept has been corroborated by Barlow (7) and Mackenzie (109). The former was uncertain whether the toxicity of the infection or the mental aberration during the period of illness was responsible for the symptoms. The latter believed that most cases could be traced back to undue exertion during some febrile disorder of which diarrhoea was the most common. Several modern writers disagree with the above concepts (180, 55).

The following table compiled by the author is based on data obtained by Da Costa, Barlow and Lewis. The data were obtained from case histories of patients with Neurocirculatory Asthenia. The illnesses mentioned are those which might have had a direct bearing on the individuals' symptoms because of the proximity of the illness to the onset of the syndrome.

	Da Costa (39) cases	%	Barlow (7) cases	%	Lewis (103) cases	%
Rheumatic fever			7	3.7	127	23
Undiagnosed fevers	34	17	29	15.6	69	12
Pleurisy			16	8.6	16	3
Pneumonia					34	6
Diarrhoea	61	38.5				
Enteric fever					43	8
Tonsillitis					45	8
Dysentery					33	6
Trench fever			17	9.15	5	1
Venereal Disease					13	2
Miscellaneous			14	7.5	87	16

These figures do not establish that infection is the cause of Neurocirculatory Asthenia, but rather imply that various infections may be prodromal to Neurocirculatory Asthenia.

7. Thyroid.

So striking is the similarity of symptoms between Neurocirculatory Asthenia and mild hyperthyroidism that several observers have thought them to be one disease entity (10, 24, 153). These views have been upheld by the recent work of Moschcowitz and Bernstein (123). The latter two men have observed eleven cases which tended to exhibit a transition from Neurocirculatory Asthenia to hyperthyroidism and vice versa. Moschcowitz and Bernstein feel that their conclusions are justifiable on the ground that both syndromes manifest signs of autonomic imbalance (20, 95).

The evidence which has accumulated during the past twenty years is opposed to such a broad conclusion. Lewis (103)

and Grant (59) have shown that normals and patients with Neurocirculatory Asthenia develop hyperthyroidism in equal proportions. Furthermore, Lewis has shown that in the Neurocirculatory Asthenia patient the hands are reddish-blue, cold and wet with perspiration in contrast to the hyperthyroid patient whose hands are reddish-white, warm and wet with perspiration.

Cohn (31) has demonstrated that the tremor in Neurocirculatory Asthenia is coarse, irregular and fluctuates greatly after exercise, while the tremor in hyperthyroidism is fine, regular and the rate being eight vibrations per second.

The blood and pulse pressures in Neurocirculatory Asthenia differ markedly from the blood and pulse pressures in hyperthyroidism. The systolic blood pressure of each group may at first approximate each other being usually 150-160 mm. Hg. However, during a day or so of rest, the systolic blood pressure in Neurocirculatory Asthenia usually drops 15-20 mm. mercury, while in hyperthyroidism, the drop is not as great. The diastolic pressure in Neurocirculatory Asthenia is usually 15-20 mm. mercury higher than the diastolic pressure in hyperthyroidism. The pulse pressure is higher in hyperthyroidism and the phenomenon of collapsing pulse is usually observed.

There is no constant basal metabolism rate reading for Neurocirculatory Asthenia, while in hyperthyroidism the basal metabolism rate is usually elevated above 40. Freidlander and Freyhof (55) observed ten cases of Neurocirculatory Asthenia with basal metabolism rates above zero and 40 cases with basal metabolism rates below zero. Similar results were observed by Peabody et al. (134-136), who found twenty-five cases of Neurocirculatory Asthenia with increased basal metabolism rates and

thirty-four cases with decreased basal metabolism rates. Aronovitch (127) reported that basal metabolism rate readings in Neurocirculatory Asthenia "were in most cases somewhat higher than normal, although not usually outside of normal limits." Kessel and Hyman (95) have observed a comparatively stable basal metabolic rate in Neurocirculatory Asthenia as opposed to a progressive rise in the basal metabolic rate as is invariably seen in hyperthyroidism.

From the evidence submitted, it is reasonable to conclude that Neurocirculatory Asthenia and hyperthyroidism are not one disease entity even though they both may show signs of autonomic imbalance, such as perspiration, tachycardia and "nervousness". In mild cases Neurocirculatory Asthenia and hyperthyroidism may resemble each other, but it is not reasonable to conclude that fully developed cases of Neurocirculatory Asthenia resemble fully developed cases of hyperthyroidism.

8. Hyperadrenalism.

When injected intravenously into individuals, doses exceeding 1 cc. of 1/1000 solution of adrenalin produce physiological changes, such as sighing respirations, tachycardia, increased blood pressure, tremor, headache and possibly bluish-red, cold, clammy extremities. Because these signs parallel those frequently observed in Neurocirculatory Asthenia, several investigators (3, 37) contended that Neurocirculatory Asthenia is due to the constant over-stimulation of the sympathetic nervous system by the adrenal medullae.

Crile (37) was so ardent in his views that he attempted to cure or alleviate the symptoms of Neurocirculatory Asthenia by bilateral adrenal medullectomy. His results, in the opinion

of those who followed his work closely, were neither curative nor palliative (29, 85, 127). These men believe that in Crile's so-called cured or improved cases, fears which were formerly directed to the cardiovascular and respiratory systems, were projected post-operatively to the site of operation and thus they were neither cured nor improved. These same men (29, 85, 127) failed to reproduce the symptoms of Neurocirculatory Asthenia in quiescent patients with Neurocirculatory Asthenia by administering various doses of adrenalin from 0.5 cc. to 2.0 cc. (1/1000 solution).

Cameron recently has offered an hypothesis that hyper-activity of the adrenal-sympathetic nervous system is responsible for the continuance of symptoms in three types of anxiety neurosis. One of these types has many of the features of Neurocirculatory Asthenia. It is "a group in which anxiety symptoms appear as a consequence of long continued exposure to a difficult and trying situation, such as is represented by battle experience or by a conflict situation in civilian life in which the anxiety symptoms do not subside on removal from danger or on termination of the conflict situation".

Cameron has succeeded in effacing the symptoms in six out of ten patients and improved the remaining four by his adrenalin desensitization technique (25).

This is by no means conclusive that the type of anxiety neurosis mentioned above is caused by the individual's sensitive-ness to adrenalin, for many patients of "anxiety neurosis" have been "cured" by intravenous or subcutaneous injections of normal saline and distilled water. By the same token, even though the type of anxiety neurosis described above and Neurocirculatory Asthenia have much in common, one cannot say with certainty, on

the basis of Cameron's work, that the "anxiety symptoms" in Neurocirculatory Asthenia are due to the patient's extreme sensitivity to adrenalin.

It may well be said that adrenalin may produce some of the symptoms of Neurocirculatory Asthenia, such as tachycardia, increased respirations and reddish-blue extremities, but it is by no means the cause of Neurocirculatory Asthenia.

9. Hyperventilation.

Henderson (74) observed that rapid breathing with a steady reduction in the alveolar carbon dioxide produced a sequential pattern of events which finally terminated in tetany. The normal value of CO_2 content in alveolar air is 5.3 volumes percent; when this decreases to about 3.5 volumes percent, the following subjective signs occur: dizziness, faintness, apprehension, nausea, numbness and tingling. As the CO_2 content in the alveolar air drops to about 2.7 volumes percent, tremors in various parts of the body and general tightening of the muscles are visible.

When tetany was proven to be the last link in a chain of physiological changes which are produced by artificial hyperventilation (32, 40, 75, 159), several clinicians observed that hyperventilation was the cause of the heretofore inexplicable syndrome occurring in hysterical and neurotic individuals (9, 58, 94, 100).

With this as their basis, Soley and Shock (148) attempted to reproduce the symptoms of Neurocirculatory Asthenia in patients with Neurocirculatory Asthenia. They reproduced many of the symptoms in each of their experiments. Their ideas about the relationship between Neurocirculatory Asthenia and hyperventilation is epitomized in the following quotation from their publication on the subject:

"The respiratory alkalosis resulting from hyperventilation produces the symptoms of effort syndrome". Soley's and Shock's theory has been questioned by Wood (178) Guttman and Jones (67) and Jones and Scarisbrick (88) who investigated it. This doubt is further strengthened by Christie's (30) observation that hypoventilation is frequently seen in Neurocirculatory Asthenia.

The main symptoms of Neurocirculatory Asthenia are dyspnoea, effort trouble, "attacks", palpitations and chest pain (60). These symptoms are present in over 94% of all observed cases of Neurocirculatory Asthenia. Other signs such as dizziness, headache, and nausea are present in approximately 60% of cases. Any good attempt to reproduce the symptoms and signs of Neurocirculatory Asthenia must reproduce the former group of symptoms. A close analysis of Soley's and Shock's results reveals that they did not produce the main symptoms of Neurocirculatory Asthenia in more than 10% of their cases (67).

Data supporting The Soley and Shock theory is not conclusive. The data is based on the association of hyperventilation with the following bodily disturbances: pain (141), emotions (74), palpitations (112), anxiety or sinking feelings(52), heat (99), psychoneurotic patients (52, 58) and those in poor physical condition (58) during exercise. Hyperventilation during the aforementioned conditions is physiological.

Experimental hyperventilation was attempted in eight patients with Neurocirculatory Asthenia in this laboratory. While several of the minor symptoms of Neurocirculatory Asthenia were reproduced, the most important symptoms i.e. cardiac pain and dyspnoea were lacking. The following is a resumé of the results obtained.

	Number present
Cyanosis	8
Dizziness	8
Headache	8
Muscular tremor	8
Increase in pulse rate	8
Numbness	7
Paraesthesia	7
Cardiac pain	0
Palpitation	0
Nausea	6
Chvostek's sign	5
Trousseau's sign	8
T_2 Wave increase	5
T_2 Wave decrease	3
S-T_2 depression	2

The average pH prior to hyperventilation was 7.35 while the average pH during tetany was 7.53.

Certain conclusions concerning hyperventilation and Neurocirculatory Asthenia may be made from the foregoing facts:

1. Neurocirculatory Asthenia is a clinical entity which is not entirely caused by hyperventilation.

2. The cause of some of the lesser symptoms of Neurocirculatory Asthenia such as dizziness, headache, tingling and nausea may be due to hyperventilation.

3. There is a definite clinical syndrome in psychoneurotics produced by hyperventilation. The salient features are increased respirations, cyanosis, muscular tremor and terminating in tetany. This syndrome should not be confused with Neurocirculatory Asthenia.

9. Psychic Factors.

Close studies of anxiety states and patients with Neurocirculatory Asthenia indicate that the two syndromes have many features in common particularly those related to sympathetic overactivity such as sighing, respiration, fainting, diarrhoea and indigestion (29). So interwoven are the two syndromes that Grinker (64) refuses to recognize Neurocirculatory Asthenia as a disease entity. He believes that cardiac symptoms in the combat man are only one form of a repressed state. In the last war he states that the manifestations of a repressed state took the form of cardiac symptoms. In this war, gastrointestinal manifestations accounted for 46.6% of all the symptoms of a repressed state, while cardiac manifestations accounted for only 14.6% of all the symptoms of a repressed state.

Intense studies of psychoneurotic patients indicate that there are a greater number of unusual and subnormal chacteristics in their personalities as compared with normal well-balanced individuals. A similar condition appears to exist in the families of these two groups (29).

Analytical personality studies of patients with Neurocirculatory Asthenia and their progenitors reveal many of the unusual and subnormal characteristics which are found in psychoneurotic patients (29).

The paragraphs to follow will compare the familial and personal characteristics of the patient with Neurocirculatory Asthenia with those of normal and psychoneurotic individuals.

Family History.

People who have studied this disease are aware of the fact that the incidence of anxiety neurosis, psychosis, insanity

and epilepsy is higher in families with Neurocirculatory Asthenia than in normal families (129, 131, 177, 180, 181).

The following table, taken from Oppenheimer and Rothschild (129), indicates that certain unusual and abnormal characteristics listed below are more frequently observed in neuroses and in Neurocirculatory Asthenia than in normal controls. This study would suggest that the parents of patients with Neurocirculatory Asthenia are constitutionally inferior as compared with the parents of normal individuals.

	Neuroses % Characteristics	Irritable Heart % Characteristics	Wounded Controls % Characteristics
Nervousness	64	45	15
Alcoholism (parents and grandparents)	50	15	24
Teetotalers (parents and grandparents)	30	15	16
Irritability of temper	36	27	12
Insanity	34	23	0
Epilepsy	30	15	0
Tuberculosis (immediate family)	12	13	4
Tuberculosis (relatives)	10	17	4
Onychophagia; adherent ear lobes	5	15	0
Positive history for one or several of above characteristics	74	56	38

Wood (180), Kozol (97) and Yaskin (181) also report a higher incidence of psychoneuroses in the family background of patients with Neurocirculatory Asthenia. There appears to be no

doubt that the parents of most patients with Neurocirculatory Asthenia do show defective behaviour characteristics.

The following passage taken from Willius (171) reveals that patients influence the lives of their offspring. "Heredity is a very important influence in forming individuals whose temperament and psychic reactions are such that development of a neurosis is relatively simple. Undesirable traits and characteristics are unfortunately as frequently transmitted to progeny as are the sterling qualities that embody the eugenic ideal. A parent of poor nervous stability, who is given to emotional outbursts in meeting the usual problems of life, sets an example for his children, which may do much in blazing a trail for the development in them of a lack of poise in their later years." Since the parents of patients with Neurocirculatory Asthenia have a greater proportion of subnormal characteristics than do the parents of normal individuals, it is reasonable to assume that patients with Neurocirculatory Asthenia will inherit more subnormal characteristics than will normals.

Personal Factors.

In discussing personal factors of patients with Neurocirculatory Asthenia, the question comes to mind whether or not the adult behaviour pattern has its basis during the formative years. The psychiatric history of these patients reveals an unusual behaviour pattern. In childhood, they are frequently timid and delicate and have a tendency to cling to their mothers. During their pre-school and early school days, such peculiarities as phobias, tics, bed-wetting, nightmares and stammering are the common occurrences (48).

Dunn (48) believes that these neurotic manifestations are a direct result of the parental influence. Wood (180) believes

that effort-intolerance in patients with Neurocirculatory Asthenia begins during puberty, due to some misinterpreted remark of a physician and because of a super-sensitive outlook.

Psychoanalytic personality tests, such as the Minnesota Multiphasic Personality Inventory (128) and Rorschach Test (142) reveal definite abnormal personality trends in cases of Neurocirculatory Asthenia.

The Minnesota Multiphasic Personality Inventory indicates that patients with Neurocirculatory Asthenia fall into the following groups (in order of prevalence):

1. Hypochondriac
2. Depression
3. Hysteria
4. Psychasthenia
5. Schizophrenia

After an analysis of the personality of Neurocirculatory Asthenia by means of the Rorschach test, Ross (142) states that the patient's personality changes are similar to those most commonly found in psychoneuroses and organic brain diseases. The salient features of the personality of the patient with Neurocirculatory Asthenia according to Ross (85) are:

a) "He gives up easily in face of emotional difficulty."

b) "Sexually disturbing stimuli do not constitute as important a difficulty as for miscellaneous psychoneurotics."

c) "An accumulation of emotional stresses is also hard to handle."

d) "Overly systematic, periectionistic."

d) "Tendency to limit perfcrmance."

f) "Unable to analyze total situation."

The manner in which the patient with Neurocirculatory Asthenia reacts to painful stimuli is a fairly good indication of his comparative inability to withstand discomfort. The patient with Neurocirculatory Asthenia is unable to match the normal individual in any one of the three tests listed below (128).

a) Level of reaction to pain. Patients and controls were asked to sit erect and carefully controlled heat was allowed to penetrate their brows. A wince or withdrawal from the heat was considered to be the end point of the test. Patients were able to withstand .315 gm. calories/20c/Cm^2, while controls were able to withstand .435 gm. calories/20c/Cm^2.

b) Dynamometer test. The maximum grip of patients and controls was determined by means of a spring dynamometer. Each individual patient and control was then asked to maintain sixty percent of his maximum grip for as long as he could. Patients were able to maintain their grip for 30.5 seconds, while normals maintained their grip for 48.8 seconds. It is interesting to note that patients were able to maintain their grip 62.5% as long as controls when gripping a spring forty percent as strong.

c) Electric shock. A pulsating electric current passed through the fingers of both groups. Each subject was asked to hold out as long as possible. Twenty-nine patients endured on the average 2.5 units of electricity, while fifty normals could stand on the average 6 units of electricity.

It has been stated on numerous occasions that patients with Neurocirculatory Asthenia have more unusual and abnormal characteristics in their personalities than have normal

individuals. This contention is clearly shown in the table which follows. This table combines the findings of Oppenheimer and Rothschild (129) and Wolfson (177), lists various characteristics which are often found in healthy people and shows the percentage relationship of these characteristics in wounded soldiers, patients with Neurocirculatory Asthenia and neuroses. The majority of these characteristics are evident in neuroses and Neurocirculatory Asthenia cases. A few of these characteristics, such as eneuresis, celibacy, frights in childhood are more frequently found in patients with Neurocirculatory Asthenia.

III. PHYSIOLOGICAL STUDIES OF PATIENTS WITH NEUROCIRCULATORY ASTHENIA AND NORMAL INDIVIDUALS.

There is no known pathological process which is directly responsible for Neurocirculatory Asthenia, and if there is no pathological process, could a disturbance in the normal physiological and psychical processes produce such a distinct clinical entity? Let us look for the answer in a study of the physiological and psychical processes in the patient suffering from Neurocirculatory Asthenia.

Tests.

1. Apnoea Time.

The length of time an individual is able to hold his breath is known as Apnoea time.

Apnoea time may be increased by adopting measures which tend to prevent the accumulation of carbon dioxide. A few of these are:

1. Hyperventilating for 30 seconds prior to the test to remove CO_2 from the alveolar air.

2. Hyperventilating and taking a full inspiration of pure oxygen prior to the test.

3. Under resting conditions.

4. Constant practice.

Drury (47) recorded the Apnoea time in healthy male soldiers and those suffering from Neurocirculatory Asthenia. The tests were performed under resting conditions and without preparation. Drury recorded that the average Apnoea time in the patients with Neurocirculatory Asthenia was 10.6 seconds, while the average Apnoea time in the controls was 45.0 seconds.

In a series of twelve patients under conditions similar to those of Drury, the average Apnoea time was 57.6 seconds, ranging 15.2 to 90.4 seconds according to Hoff, Hunn and Gertler (79).

Aronovitch (127) found that normal individuals under resting conditions and without preparation, may hold their breath for an average of 55.3 seconds before prolonged schedule of physical training and 65.3 seconds after completion of the schedule of physical training.

Wood (179) found in a series of two hundred cases of Neurocirculatory Asthenia that the Apnoea time under resting conditions without preparation was 21 seconds. Twenty-four per cent of these cases had an Apnoea time of 30 seconds or over.

2. Vital Capacity.

The total amount of air which can be exhaled after a maximal inspiration is called Vital Capacity (15).

Dreyer (46) observed that vital capacity varies with the occupation of the individual. The more sedentary the occupation, the less will be the vital capacity and vice versa.

Peabody (136) learned that the vital capacity has to be reduced sixty per cent of the normal value before dyspnoea on exertion or constant dyspnoea occurs. Levine and Wilson (101) found that vital capacity in Neurocirculatory Asthenia was slightly reduced, i.e. two per cent in moderate cases of Neurocirculatory Asthenia and eleven per cent in severe cases of Neurocirculatory Asthenia. After drills the vital capacity of patients with severe Neurocirculatory Asthenia drops about eight per cent and after exhausting exercises drops about nineteen per cent. In the author's series of pre- and post-exhaustive tread-mill

exercises executed by seven individuals, we found an average vital capacity of 3880 and 3720 cubic centimeters, respectively(79). This represents a reduction of five per cent in vital capacity after exhaustive exercises. Adams and Sturgis (1) observed a reduction of ten per cent in vital capacity in soldiers with Neurocirculatory Asthenia after exhaustive exercises.

Canadian Army medical reports reveal that with graded physical training the vital capacity of "pre Neurocirculatory Asthenia soldiers" may be improved from four to eleven per cent (127).

3. Pulse Rate (Heart beats per minute).

Wood (179) found an average of eighty-two beats per minute during routine daytime examination of two hundred patients with Neurocirculatory Asthenia (range 48 - 136), while fifty-six normal subjects showed an average heart rate of sixty-six beats per minute (range 48 - 100). Hume (85) observed that during sleep patients with Neurocirculatory Asthenia had an average pulse rate of 60 - 65 beats per minute. This is the same rate reported by Boas and Goldsmith (18) in normal individuals.

Parkinson (132) showed that the pulse rates of patients with Neurocirculatory Asthenia were higher than normal subjects by five, eleven and seventeen beats during rest, standing and exertion respectively.

Meakins and Gunson (119) corroborated Parkinson's results and added that infections and bed rest increased the pulse recovery time in the cases with Neurocirculatory Asthenia.

The pulse recovery time as defined by Meakins and Gunson is the time required for the pulse to return to its

initial resting level after the individual has marched 100 yards at 120 paces to the minute followed by an ascent of 30 "ordinary" stairs.

Bass and Wessler (12) found a rise of forty-eight in the heart rate of children with Neurocirculatory Asthenia and a rise of fifty in the heart rate of normal children during "exercise". Wood (179) tested patients with Neurocirculatory Asthenia and control subjects by the Meakins and Gunson test (119). Averaging his results with those obtained by Meakins and Gunson, he reported a rise of 39.8 beats per minute in Neurocirculatory Asthenia and 40.4 beats per minute in controls.

4. Treadmill Tests.

One of the chief complaints of the patient with Neurocirculatory Asthenia is his inability to do hard work. White et al. (128) adopted the human treadmill to measure the amount of work which could be done by patients and controls under similar conditions. The treadmill was inclined at 8.6 degrees and allowed to run at seven miles per hour. Forty-three patients averaged 79.6 seconds on the machine, while sixty-three control subjects averaged 201.6 seconds (128).

This test does not give conclusive proof of the inability of patients with Neurocirculatory Asthenia to do hard work, but, according to the report (128), the results have been calculated to be statistically significant.

5. Fatigue Laboratory Index.

This test was introduced by Johnson, Brouha and Darling (87). The general requirements are exercises that will exhaust sixty-five per cent of any given group within a period of five minutes. The exercise must involve large muscle groups. Johnson,

Brouha and Darling believe that running uphill satisfies all these conditions. The materials required for the test are a stop watch and a competent observer. The subject "works" until he is exhausted or for a period not longer than five minutes. The pulse rate is taken upon recovery from one to one and a half minutes, from two to two and a half minutes and from four to four and a half minutes. The index of fitness for hard work

$$\text{equals} \quad \frac{\text{Duration of exhaustion work in seconds} \times 100}{2 \times \text{sum of pulse from } 1 - 1\frac{1}{2},\ 2 - 2\frac{1}{2} \text{ and } 4 - 4\frac{1}{2} \text{ minutes after work}}$$

The larger the score, the better the subject; any score above one hundred is considered good.

Cohn et al. (128) modified this test by adding the recovery pulses at one minute, two minutes and four minutes in each of four sets of exercises given to patients with Neurocirculatory Asthenia and control subjects. In all four sets of exercises the sum of the patients' recovery pulses were markedly higher than those of the normal subjects.

Exercise	Patients	Controls
1.	265	225
2.	270	250
3.	265	240
4.	300	250

The scores in the modified test do not have the same significance as the Johnson, Brouha and Darling test. The higher the score in the former, the lower is the adaptability for work, while the opposite is true in the latter.

6. The Harvard Step Test.

The cardiovascular efficiency tests proposed by Parkinson (132), Kahn (89), Meakins and Gunson (119) were only useful and helpful in comparing an isolated group of patients and normals.

The Harvard step test, which is now being used widely, standardizes the amount of work so that all results can be compared adequately. The procedure of the test is as follows: The individual climbs and descends a step twenty inches in height thirty times a minute for a period not longer than five minutes. The physical fitness index

$$\text{equals} \quad \frac{\text{Duration of exercise in seconds x 100}}{\text{2 x sum of pulse counts from 1 - 1.5, 2 - 2.5 and 3 - 3.5 minutes after cessation of exercise}}$$

Scores of one hundred are considered good. Any score below seventy-five is considered poor. Ten patients with Neurocirculatory Asthenia tested in this way in this laboratory scored on the averaged 73.5 with ranges from 70 to 85.

7. Cardiac Output.

The only cases on record of cardiac output in Neurocirculatory Asthenia are those of Starr. Starr (150), using his ballistocardiographic technique, has suggested that the cardiac output in patients with Neurocirculatory Asthenia is increased. There are no concrete values for cardiac output given in his work, nor has anyone corroborated his results. No definite conclusion should be drawn from Starr's results until further evidence is submitted using more patients with Neurocirculatory Asthenia and control subjects.

8. Circulation Time.

Spillane (174), using the saccharin method, noted that

the circulation time in twenty-seven out of thirty soldiers suffering from Neurocirculatory Asthenia was normal. He also noted that the circulation time in patients with Neurocirculatory Asthenia did not change greatly after exercise.

9. Lactic Acid.

Cohn and White (128) suggested that the accumulation of lactic acid in the blood after moderate exercises is higher in patients with Neurocirculatory Asthenia than in normal individuals, while the reverse appears to be true after exhaustive exercises. The former fact is in accord with other views (43, 70), while the latter is open to question. It is believed, on the basis of work done in this laboratory employing the human treadmill, that the explanation for the lower blood lactate level in patients with Neurocirculatory Asthenia after exhaustive exercises is as follows.

Normally the point of exhaustion is at a pulse rate of 180. A well-trained athlete will have a pulse rate of about 60 prior to exercise and his pulse rate will gradually rise to the exhaustive level of 180. During this time lactic acid will be accumulating in the blood. The blood lactate level will rise in proportion to the time required to produce exhaustion and the rate of removal of lactic acid from the blood stream. These two factors could account for a comparatively high blood lactate level in a well-trained athlete after exercise.

In patients with Neurocirculatory Asthenia the pulse rate prior to exercises is usually around 85 to 90. Since they are usually in poor or fair physical condition (128), the pulse rate rises quickly to the point of exhaustion. The accumulation of lactic acid may be slight, due to the brevity of the time

required to produce exhaustion, balanced perhaps by a poor mechanism for the removal of lactic acid from the blood stream. Another factor must be considered in Neurocirculatory Asthenia. Often these individuals complain of exhaustion before they actually are or should be exhausted according to their pulse rates. This will tend to decrease the time during which the lactic acid will accumulate in the blood stream and hence may help to account for the low blood lactate level in these patients. The following are the actual results obtained by Cohn and White:

	Normals	Neurocirculatory Asthenia
Lactic Acid mgs. per 100 cc. blood Moderate exercise	21.4	36.4
Lactic Acid mgs. per 100 cc. blood Exhaustive exercise	122.7	77.1

The accumulation of lactic acid in the blood has been thought to be the limiting factor of cardiac activity as evidenced by the higher resting level of blood lactic acid in cases of cardiac decompensation (70) and the comparatively low level of lactic acid in the well trained athlete at rest (43). The results obtained by White (128) appear to imply that the cardiac condition in Neurocirculatory Asthenia is due to the increased accumulation of lactic acid in the blood stream.

In order to test the validity of the concept that lactic acid is the limiting factor in cardiac metabolism and hence activity (107), 0.1N lactic acid was injected intravenously into sixteen dogs until cardiac activity ceased. It was observed that the degree of impairment of the cardiac activity was a function of

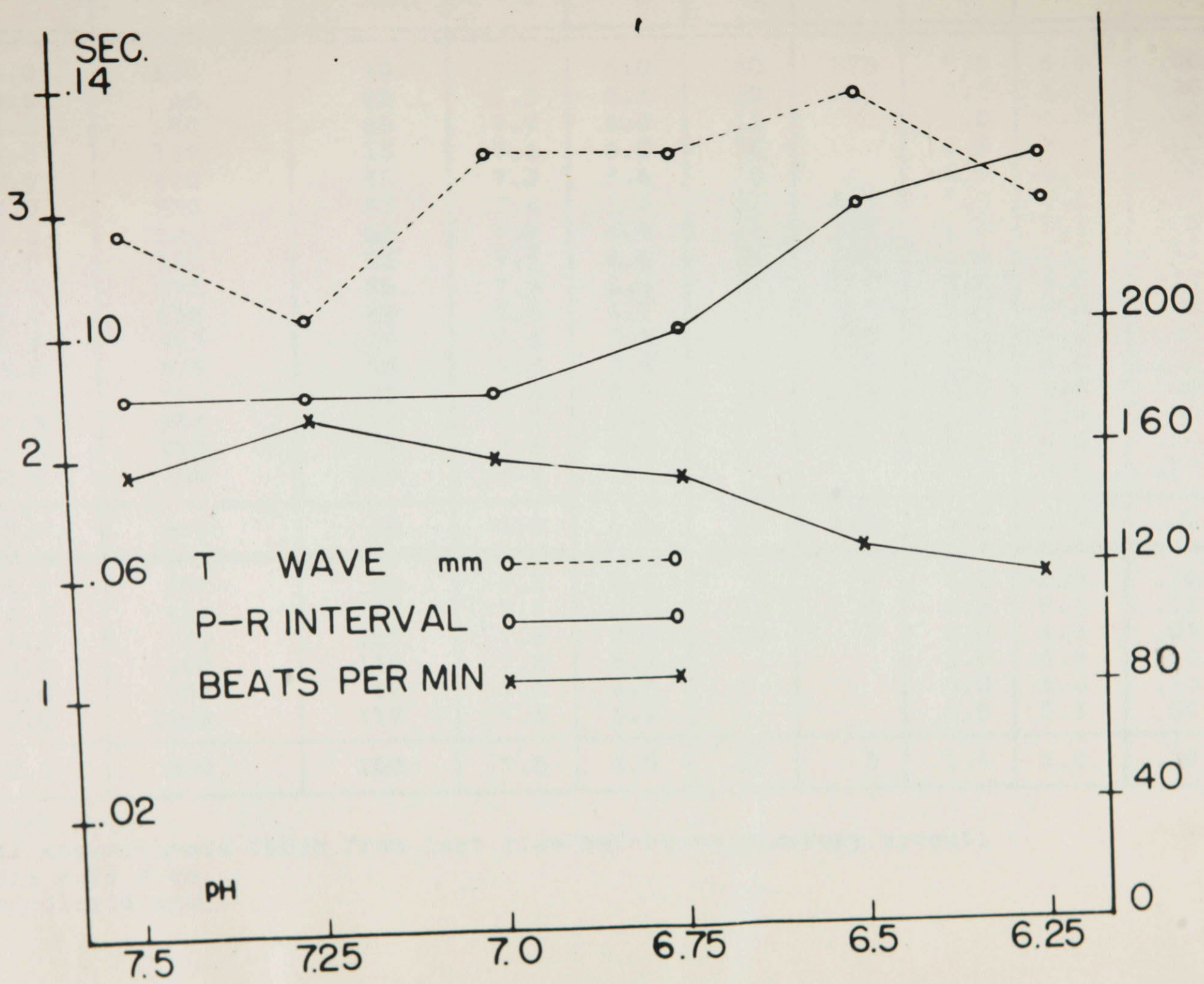
the degree of blood acidity and bore no evident relationship to the blood lactate level. Cardiac activity ceased on the average at pH 6.25.

In order to further substantiate these observations, two other sets of experiments were done. In the first type of experiment, one dog was injected intravenously with 0.1N sodium lactate. No significant change was recorded in the blood pH, but blood lactate levels rose to 525 mgs. per cent. Cardiac activity was unimpaired and death occurred because of water intoxication as evidenced by pulmonary and cerebral oedema.

In the second type of experiment 0.1N HCl was injected intravenously into ten dogs until cardiac activity ceased. The average blood pH at this point was 6.25 with ranges from 5.75 to 6.75. It was noted that the blood lactate levels were lower as the experiment proceeded and that the degree of impairment of cardiac function was a function of the degree of blood acidity.

From the foregoing facts it is impossible to uphold the hypothesis that the cardiac symptoms in Neurocirculatory Asthenia are due to faulty oxidation of lactic acid and its accumulation in the blood. Assuming that this were so, the amount of lactic acid which would accumulate in the blood and hearts of patients with Neurocirculatory Asthenia would be insignificant in comparison with the amount required to produce the changes in blood pH necessary to alter the cardiac function.

The table to follow is the result obtained in the experiments cited above. These are summarized in Graph No. 1.


SEC.
.14
3
.10
2
.06
1
.02
200
160
120
80
40
0
T WAVE mm
P–R INTERVAL
BEATS PER MIN
pH
7.5
7.25
7.0
6.75
6.5
6.25

Dog No.	Weight kilos	Amount acid injected cc.	Time of Expt. min.	pH artery		Mgs. % Lactic acid		Height of T wave mm.		P-R sec.	
				I	F	I	F	I	F	I	F
A 1	6.0	120	40	7.4	6.0	30	275	2.5	4.0	.08	.11
2	3.5	68	22	7.5	6.1	20	210	3.3	4.5	.08	.12
3	4.5	86	26	7.7	6.0	11		1.0	2.5	.08	.13
4	4.5	127	15	7.4	6.0	10		4.3	7.8	.08	.09
5	20.0	450	66	7.3	6.4	0		-2.5	-2.0	.08	.10
6	12.0	535	85	7.4	6.5	12	220	7.0	9.0	.12	.11
7	12.0	200	29	7.7	6.6	14	190	-1.5	3.5	.09	.10
8	7.0	150	23	7.3	6.4	11	189	-1.0	5.0	.11	.13
9	6.5	375	78	7.5	5.6	21	350	2.5	5.0	.09	.12
10	6.0	450	88	7.5	6.7	28	317	2.0	5.0	.12	.12
11	25.0	975	107	7.3	5.9	27	293	4.5	4.0	.09	.12
12	13.0	375	70	7.5	5.9	15	395	2.0	3.0	.11	.16
13	25.0	550	103	7.3	6.6	18	280	4.3	3.0	.08	.09
14	27.0	900	114	7.3	6.6	32	250	-1.5	3.0	.08	.10
15	9.0	380	79	7.4	6.2	15	172	3.0	3.0	.08	.10
16	28.0	950	129	7.4	6.4			-2.0	6.0	.08	.12
Aver.	13.5	400	58	7.4	6.2	19	262	1.3	3.7	.09	.11
B 1	5.5	475	60	7.5	5.8	4	8	1.0	-2.5	.10	.16
2	14.0	450	56	7.7	5.9	35	8	2.5	2.5	.11	.16
3	14.5	750	127	7.6	5.8	12	7	2.0	4.0	.09	.17
4	20.0	1400	155	7.3	6.2			1.0	4.0	.10	.10
5	12.0	858	87	7.4	6.3			2.0	2.5	.10	.12
6	12.0	1100	117	7.4	5.9			2.5	5.3	.09	.13
Aver.	13.0	839	100	7.5	5.9	17	8	1.6	3.0	.10	.14

I - Initial value.
F - Final measurements taken from last view before respiratory arrest.
A - Lactic acid dogs.
B - Hydrochloric acid.

10. Hyperventilation and the Electrocardiogram.

It has been suggested that in patients with anxiety neurosis and the hyperventilation syndrome frequently exhibit electrocardiographic changes consisting of a late inverted T wave or S-T depression (158). These electrocardiographic changes disappear upon recovery. Similar electrocardiographic changes have been produced by the ingestion of sodium bicarbonate (6), and voluntary hyperventilation (6, 98, 158).

Barker et al. (6) believe that the diminution in height or inversion of the T wave is more closely related to pH than to carbon dioxide combining power of the blood lactic acid acid, serum calcium or potassium. This contention is supported by the observations of Kronenberger and Ruffin (98) that in hyperventilation there is alkalosis, diminution in the height of the T wave, while during exercise there is acidosis and increase in height of the T wave. These observations have been corroborated by other investigators (6, 11, 158), one of whom (6) produced an increase in the height of the T wave by administering twenty-five grams of ammonium chloride orally.

There is evidence which weakens the belief that electrocardiographic changes are due primarily to the degree of pH. Other factors, such as the level of serum potassium and calcium and the degree of chest expansion (71) during hyperventilation or exercise, must not be overlooked.

It is impossible to single out the cause of the T wave changes during hyperventilation because each of the

variables, such as potassium, calcium, blood lactate and CO_2 combining power may each prolong or abbreviate repolarization in either ventricle.

It is, therefore, justifiable to conclude that there is no diagnostic electrocardiographic pattern of the hyperventilation syndrome that is frequently associated with or mistaken for Neurocirculatory Asthenia.

11. The Wendkos Test.

After a study of sixty patients with Neurocirculatory Asthenia, Wendkos (164) concluded as others did (106, 166) that there is no change in the three conventional electrocardiographic limb leads in Neurocirculatory Asthenia. Wendkos employed the precordial leads CF 2 and CF 4, standardized and adopted by the American Heart Association (155) and found that inversions of the T waves in these latter leads were significant. Moreover, he could categorize the cases of Neurocirculatory Asthenia which were predominantly vagotonic and sympathecotonic. His criteria for such grouping are as follows:

Vagotonic T

1. Any T wave that is exaggerated to begin with and is further exaggerated by a sympatholytic drug such as ergotamine.
2. Any T wave that is exaggerated to begin with and abolished by:
   a) parasympatholytic drug (atropine)

b) sympathomimetic drug

c) upright position.

Sympathotonic T

1. Any T wave that is exaggerated to begin with and is normalized by a sympatholytic drug.
2. Any T wave that is exaggerated to begin with and is further exaggerated by:

   a) sympathomimetic drug

   b) upright position.

This study is still in its infancy, but the possibilities of the practical use of this test are great.

12. The Tilt-Table Test.

The tilt-table studies in this laboratory were originally started by Captain H. Stansfield under the direction of Professor H. E. Hoff. Captain Stansfield was posted elsewhere after completing electrocardiographic studies on twenty normal subjects. Captain Stansfield was replaced by Captain D. Best who in turn was replaced by Captain P. Weil. Captain Best was able to complete, during his brief stay here, electrocardiographic studies on six patients with Neurocirculatory Asthenia and ten patients with cardiovascular disease. Captain P. Weil secured the remaining twelve patients with Neurocirculatory Asthenia employed in this study from the military authorities. The author is very grateful to Captains Stansfield and Best for allowing their work to be included in this thesis.

To Captain Weil the author is extremely indebted for his constant co-operation and assistance in securing patients.

An electrocardiogrphically controlled tilt-table test was introduced in 1943 by Bartlett to segregate quickly cases of Neurocirculatory Asthenia from "anxiety neurosis, neurasthenia and psychasthenia" (12). Bartlett believed that by a change in the posture of his subjects from the dorsal recumbent to a 65 degree tilt position (61) he succeeded in bringing about temporary myocardial ischemia which could be detected in the electrocardiogram by the following criteria established by Levy et al. (102): a) Deviation of the RS-T segment in leads I, II and III and 1VF totalling 3 mm. or more; b) partial or complete reversal in the direction of T in lead I if accompanied by an RS-T deviation of 1 mm. or more in this lead; c) reversal of T in 1VF regardless of RS-T deviation; d) partial reversal of T in 1VF if accompanied by RS-T deviation of 1 mm. or more in this lead. According to Bartlett the test was positive in 71 per cent of all patients with Neurocirculatory Asthenia (21 cases) and in 91 per cent of patients suffering from coronary artery disease (23 cases).

Several aspects of Bartlett's theoretical considerations are open to question. Changes closely resembling some of the electrocardiographic criteria of coronary insufficiency proposed by Levy and adopted by Bartlett have

been observed during postural changes in normal individuals (168), in fear prior to surgical operations (110), after deep breathing and in physiological axis deviation (169). In addition, inversion of T_3 has been observed normally in 20 per cent of cases (64). RS-T deviations of more than 1 mm. in any lead are known to occur during fear (4) and postural changes (110). Furthermore, RS-T elevations totalling as much as 1.43 mm. in all leads were observed in 73.5 per cent of the thousand aviators studied by Graybiel (64).

Following the sudden change in posture from the dorsal recumbent to the 65 degree tilt position, there is an increase in the diastolic blood pressure, an increase or decrease in the systolic blood pressure, resulting in a rise in the mean aortic pressure (15). Since the coronary circulation is mainly dependent upon the mean aortic pressure (15), it is reasonable to assume that impairment in the coronary flow would not result from such sudden postural changes unless reflex constriction of the coronary arteries were involved, and there is little reason to assume that this factor could occur to such a degree that anoxemia developed, particularly in view of the marked vasodilatation known to develop as a result of myocardial anoxemia. From the foregoing considerations it is difficult to accept the view that the electrocardiographic changes described by Bartlett developed because

of an impairment in coronary blood flow.

The need for an accurate clinical test by which Neurocirculatory Asthenia and coronary artery disease could be segregated from other illnesses is obvious, however, and Bartlett's work was therefore repeated in part and extended to include with cardiac disease an equal number of normal subjects chosen to constitute an age group control.

Materials and Methods

The electrocardiographic responses to postural changes were studies in four groups of subjects as follows:

1. Twenty-six normal subjects which included twenty-three males and three females whose age varied from 19 to 28. These served as controls for the patients with Neurocirculatory Asthenia. These subjects were chosen at random from the students and staff of McGill University and were, as far as could be determined by a history and physical examination, in normal health.

2. Eighteen male patients with Neurocirculatory Asthenia. These cases were carefully selected by physicians of the R.C.A.M.C. and conformed to the classical criteria upon which the diagnosis of Neurocirculatory Asthenia is made (180). These include a history of dyspnoea, effort trouble, palpitation, chest pain, nervousness and fatiguability and physical findings of an anxious expression, tachycardia, elevated blood pressure and cold, reddis-

purple extremities.

3. Seventeen male patients and one female patient with known cardiovascular disease. This group included five subjects with severe angina pectoris based on history, seven subjects with angina pectoris and hypertensive heart disease and five subjects who had at one time been hospitalized for a coronary episode. All five showed electrocardiographic signs of myocardial infarction.

4. Sixteen subjects served as controls to the group with known cardiac disease. These individuals were carefully selected adults who neither suffered from cardiovascular disease, nor any other illness of serious importance. These subjects were matched where possible against the cardiac patients in age, sex and stature.

Six electrocardiographic records employing the three standard limb leads were taken from each subject in the following positions using a Sandborn Cardiette with standard sensitivity: 1) at rest, sitting relaxed in an arm chair; 2) standing erect at ease; 3) dorsal recumbent on the tilt-table. Care was taken at this point to be certain that the subject showed no signs of apprehension. The state of relaxation was considered adequate when three consecutive blood pressure and pulse recordings taken one minute apart showed no variation. 4) Immediately upon assuming a tilt position of 70 degrees; 5) after the subject had remained in the tilt position for ten minutes; 6) immediately upon resumption of the dorsal recumbent position. During each period the blood pressure and pulse rate were recorded at one minute intervals throughout the test.

Measurements of each electrocardiogram were made to determine the direction and amplitude of the P, Q, R, S and T deflections, RS-T deviations, the duration of the Q-T, P-R and

TABLE I

Average of Electrocardiographic Findings in Twenty-six Normal Subjects.

	Sitting Position 1			Standing Position 2			Lying Position 3			Tilt 0 min. Position 4			Tilt 10 min. Position 5			Lying Position 6		
P wave mm.	0.8	1.4	0.8	0.7	1.5	1.2	0.7	1.3	0.8	0.6	1.7	1.3	0.6	1.6	1.5	0.7	1.2	0.8
Q wave mm.	0.3	0.4	0.7	0.2	0.5	0.7	0.3	0.4	0.5	0.2	0.7	0.8	0.1	0.6	0.7	0.3	0.3	0.3
R wave mm.	7.2	11.0	6.8	5.4	12.0	8.0	5.2	11.0	7.6	4.3	12.0	9.1	4.0	12.0	9.9	5.5	11.0	7.2
S wave mm.	1.6	1.4	1.1	1.8	1.3	1.0	1.3	1.1	0.8	1.7	1.3	0.7	1.9	1.2	0.8	1.3	1.2	0
T wave mm.	3.0	3.0	0.1	2.2	1.9	0.1	2.4	3.3	1.1	1.8	2.2	0.6	1.7	1.3	0.1	2.5	3.1	0.9
Q-T interval	.32	.32	.32	.32	.32	.32	.32	.32	.32	.32	.32	.32	.32	.32	.32	.32	.32	.32
P-R interval	.13	.13	.14	.12	.12	.13	.13	.13	.13	.13	.13	.13	.13	.13	.13	.13	.13	.13
R-R interval	.77	.77	.77	.70	.70	.70	.84	.84	.84	.74	.74	.74	.66	.66	.66	.80	.80	.80

TABLE II

Average of Electrocardiographic Findings in Eighteen Subjects with Neurocirculatory Asthenia.

	Sitting Position 1			Standing Position 2			Lying Position 3			Tilt 0 min. Position 4			Tilt 10 min. Position 5			Lying Position 6		
P wave mm.	0.6	1.6	1.0	0.6	2.0	1.3	0.7	1.5	0.8	0.6	1.8	1.4	0.6	1.9	1.4	0.7	1.4	0.8
Q wave mm.	0.2	0.4	1.2	0.0	0.7	1.2	0.1	0.4	0.8	0.0	0.5	0.9	0.0	0.5	0.8	0.1	0.5	0.8
R wave mm.	5.0	7.4	4.9	3.8	8.4	5.9	4.3	8.3	4.9	3.2	8.5	6.8	3.1	8.1	6.0	4.4	7.8	4.3
S wave mm.	2.2	1.1	0.7	2.4	0.7	0.0	2.0	1.0	0.3	2.1	1.1	0.4	2.0	1.2	0.4	1.5	1.0	0.7
T wave mm.	2.2	1.7	0.2	1.4	0.7	0.4	1.9	2.1	0.3	1.5	1.2	0.1	1.3	1.1	0.1	1.9	2.3	0.4
Q-T interval	.31	.31	.31	.30	.30	.30	.32	.32	.32	.32	.32	.32	.32	.31	.31	.32	.32	.32
P-R interval	.12	.12	.12	.12	.12	.12	.12	.12	.12	.12	.12	.12	.12	.12	.12	.12	.12	.12
R-R interval	.68	.68	.68	.65	.65	.65	.77	.77	.77	.68	.68	.68	.66	.66	.66	.76	.76	.76

TABLE III

Average of Electrocardiographic Findings in Sixteen Subjects who Served as Cardiac Controls.

	Sitting Position 1			Standing Position 2			Lying Position 3			Tilt 0 min. Position 4			Tilt 10 min. Position 5			Lying Position		
P wave mm.	0.8	1.3	0.6	0.7	1.5	0.9	0.7	1.1	0.6	0.7	1.3	1.0	0.9	1.2	1.0	0.8	1.1	
Q wave mm.	0.5	0.2	0.4	0.4	0.4	0.8	0.6	0.4	0.7	0.6	0.5	0.7	0.3	3.5	0.9	0.4	0.3	1.2
R wave mm.	7.3	8.1	3.7	5.9	6.9	4.3	5.9	8.6	4.3	5.1	8.1	5.3	5.5	2.6	5.4	5.8	8.2	5.3
S wave mm.	1.1	0.8	2.1	1.2	0.9	1.3	0.9	0.7	0.6	0.9	0.8	0.5	1.2	1.0	0.9	1.0	0.7	0.4
T wave mm.	2.9	2.9	0.3	1.8	2.0	0.2	2.4	2.8	0.9	1.8	2.2	0.6	1.9	2.0	0.2	2.2	2.7	0.6
Q-T interval	.32	.32	.32	.31	.31	.31	.32	.32	.32	.30	.30	.30	.30	.30	.30	.32	.32	.32
P-R interval	.13	.13	.13	.13	.14	.14	.13	.13	.13	.13	.13	.13	.13	.13	.13	.13	.13	.13
R-R interval	.74	.74	.74	.69	.69	.69	.78	.78	.78	.72	.72	.72	.66	.66	.66	.63	.63	.63

TABLE IV

Average of Electrocardiographic Findings in Eighteen Subjects with Known Cardiac Disease.

	Sitting Position 1			Standing Position 2			Lying Position 3			Tilt 0 min. Position 4			Tilt 10 min. Position 5			Lying Position 6		
wave mm.	0.5	1.1	0.6	0.8	1.2	0.9	0.6	1.1	0.5	0.6	1.3	0.9	0.5	1.3	0.9	0.6	1.1	C
Q wave mm.	0.3	0.3	0.5	0.3	0.5	0.5	0.3	0.2	0.4	0.3	0.4	0.3	0.2	0.4	0.3	0.3	0.2	0.4
R wave mm.	7.3	7.6	3.7	0.6	7.9	4.0	5.7	7.5	3.4	5.7	7.0	4.3	4.8	7.5	4.2	5.1	6.0	3.6
S wave mm.	0.9	0.9	2.1	1.0	1.0	1.4	5.8	1.0	1.7	0.7	0.8	1.5	0.8	0.8	1.0	0.7	1.1	1.5
T wave mm.	1.3	1.3	0.2	1.1	0.8	0.1	1.3	1.5	0.6	1.0	1.1	0.2	0.9	0.9	0.1	1.1	1.5	0.4
Q-T interval	.27	.27	.27	.28	.28	.28	.28	.28	.28	.28	.27	.26	.28	.28	.28	.27	.27	.27
P-R interval	.12	.13	.14	.13	.13	.13	.12	.12	.12	.12	.12	.12	.12	.12	.14	.12	.12	.13
R-R interval	.76	.76	.76	.68	.68	.68	.80	.80	.80	.74	.74	.74	.70	.70	.70	.78	.78	.78

R-R intervals. The measurements were accurate to plus or minus 0.2 mm. or 0.01 seconds. The results obtained were then averaged in all leads and positions for all subjects.

Results

Tables I to IV summarize the electrocardiographic measurements of the four groups in the six positions.

1. P wave changes. The maintenance of a tilt position of 70 degrees for 10 minutes had no influence on the direction of any P_1 or P_2 component. There were five inversions of P_3 in the four groups during the same period.

2. Axis deviation. The values for the directions of the electrical axis were calculated according to the method suggested by Carter, Richter and Greene (28a) (Table V). The values are within the normal range of -30 to +120 as given by Graybiel et al. (64).

In each group there was, as could be expected, a shift towards the right during the change in posture from the recumbent to the 70 degree tilt position. The maintenance of the tilt position for 10 minutes did not affect the electrical axis to any significant extent.

TABLE V

Variations in the Electrical Axis of the Heart During the Six Positions in the Four Groups of Subjects.

	Normals	Neuro-circulatory Asthenia	Cardiac Controls	Cardiacs
Sitting	+68 degrees	+70 degrees	+45 degrees	+45 degrees
Standing	79	82	55	48
Lying	74	72	55	47
Tilt 0	82	79	59	50
Tilt 10	80	75	60	57
Lying	66	62	58	51

TABLE VI

The Change in Polarity of the T Wave During the Positions in the Four Groups of Subjects.

DIRECTIONS	Sitting			Standing			Lying			Tilt 0			Tilt 10			Lying		
	T_1	T_2	T_3	T_1	T_2	T_3	T_1	T_2	T_3	T_1	T_2	T_3	T_1	T_2	T_3	T_1	T_2	T_3
NORMALS																		
Positive	26	26	17	26	25	18	26	26	23	26	26	18	25	23	13[x]	26	26	22
Negative	0	0	9	0	1	8	0	0	3	0	0	8	0	2	12	0	0	4
Isoelectric	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Diphasic	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
NEUROCIRCULATORY ASTHENIA																		
Positive	14	13	3[x]	12	10	2[x]	17	17	11	18	16	6	18	17	9	18	17	12
Negative	0	1	6	0	2	7	0	1	5	0	2	5	0	1	6	0	1	6
Isoelectric	0	0	2	1	1	1	0	0	0	0	0	2	0	0	0	0	0	0
Diphasic	0	0	3	0	0	3	1	0	1	0	0	5	0	0	3	0	0	0
CARDIAC CONTROL GROUP																		
Positive	16	16	9	16	16	10	16	16	10	16	16	9	16	16	9	16	16	10
Negative	0	0	6	0	0	6	0	0	5	0	0	5	0	0	7	0	0	6
Isoelectric	0	0	1	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0
Diphasic	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
CARDIAC GROUP																		
Positive	17	17	10	17	14	9	16	16	10[x]	16	15	8	15	15	7[x]	17	17	10
Negative	1	1	7	1	4	9	1	2	5	1	3	7	2	1	7	0	1	8
Isoelectric	0	0	1	0	0	0	1	0	1	1	0	3	0	1	3	1	0	0
Diphasic	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

[x]Remaining records not available.

3. T wave changes. Table VI is a summary of the direction of the polarity of the T waves during the six positions in the four groups of individuals. Only one instance of T_1 inversion was observed in the whole series and this occurred in a subject with known cardiac disease after maintaining a 70 degree tilt position for ten minutes. By far the greatest number of inversions occurred in T_3 at the termination of the 70 degree tilt position in the young adult group.

Even in those instances in which the T wave did not become completely negative during the change in posture from the dorsal recumbent to the 10 minute 70 degree tilt position, a decrease in amplitude of the T wave nevertheless occurred. This is illustrated in Table VII.

TABLE VII.

Percentage of Instances in which a Decrease in Amplitude of the T Wave Occurred During Postural Changes.

	Number	Lying to Tilt 0			Tilt 0 to Tilt 10			Lying to Tilt 10		
		T_1	T_2	T_3	T_1	T_2	T_3	T_1	T_2	T_3
Normals	26	68	68	68	40	76	68	80	92	72
Neurocirculatory Asthenia	18	60	82	60	27	33	50	60	88	66
Cardiac Controls	16	60	60	66	6	22	16	60	66	72
Cardiac Group	18	50	55	55	50	44	50	50	60	50

The studies of the number of inverted T waves and the decrease in amplitude of the T waves during the postural changes mentioned above, show that both the greatest number of inversions and the greatest decrease in amplitude of the T waves during the change from the dorsal recumbent to the 70 degree tilt position occur in the young adult group and in the group with Neurocirculatory

Asthenia. Fig. I illustrates the T wave changes in the three leads for all positions in the four groups of subjects.

4. RS-T deviations. The sum of the RS-T deviations in all three leads never amounted to more than one millimeter in any position.

5. Blood pressure. Generally, similar changes in the blood pressure were observed in all groups. The general pattern of behavior was that of a rise in the diastolic pressure or change from the recumbent to the tilt position with a further increase during the ten minutes of tilting. The systolic blood pressure usually fell immediately upon tilting and rose slightly during the ten minutes of tilting in the normal control and cardiac groups and fell slightly in the other two groups. These changes are illustrated in Table VIII.

TABLE VIII.

Average Blood Pressure in the Four Groups in the Various Positions.

	Initial Lying	Tilt 0	Tilt 10	Final Lying
Normals	123/75	118/82	116/88	119/75
Neurocirculatory Asthenia	134/84	130/92	132/95	130/84
Cardiac Controls	122/81	117/90	121/91	124/78
Cardiacs	138/89	135/91	134/97	137/80

6. Heart Rate. During the sitting and standing positions the heart rate was the greatest in the group with Neurocirculatory Asthenia. The heart rates in all groups save the cardiac averaged 91 after tilting 70 degrees for ten minutes. The increase in rate from the recumbent to the ten minute tilt 70 degree position was 19, 13, 14 and 11 for the normal, Neurocirculatory Asthenia,

cardiac control and cardiac groups respectively. Table IX is a summary of the average pulse rates of the four groups in the six positions.

TABLE IX.

The Average Pulse Rates in the Four Groups in the Six Positions.

	Normals	Neurocirculatory Asthenia	Cardiac Controls	Cardiacs
Sitting	78	89	81	79
Standing	86	93	87	88
Lying	72	78	77	75
Tilt 0	81	89	84	81
Tilt 10	91	91	91	86
Lying	75	79	95	77

7. Miscellaneous. Only two cases of syncope during tilting were observed; one in the normal control group and one in an elderly cardiac control subject. One or more of the following signs were usually seen in each subject during the ten minutes of tilting: perspiration, trembling, anxiety and restlessness.

Discussion

The results in these experiments fail to confirm the contention of Bartlett that patients with coronary artery disease and Neurocirculatory Asthenia show a more active response with respect to T waves and RS-T deviations than do normal subjects on change from the dorsal recumbent to the 70 degree tilt position. On the contrary, the normal control group showed a greater response to such a sudden change in posture than any of the other groups.

In addition to the electrocardiographic criteria of

coronary insufficiency proposed by Levy et al., other electrocardiographic criteria of coronary insufficiency have been suggested by Rothschild and Kissin in their anoxemia test (142) and Master et al. in their two-step test (112). These criteria are based upon RS-T deviations of 0.5 mm. or greater in any of the three standard leads (11, 12) and reversal of polarity in the T wave in any of the three standard leads (112). In general, it may be stated that the results of these experiments fail to meet the requirements of these criteria. The only electrocardiographic criterion of coronary insufficiency which the results in these experiments fulfill is that of Master, namely, the reversal of polarity in the T wave in any of the three standard leads. Bartlett's positive tests include, according to his published results, those individuals in whom a complete change of polarity in the T wave occurred in any lead. This positive sign fulfills Master's electrocardiographic criterion of coronary insufficiency (see Bartlett's charts 2, 3, 4, 5, 7 and 8).

Inversion of the T wave in lead III is found normally in 20 per cent of individuals, while inversion of the T wave in lead II is normally found in 0.2 per cent of individuals; inversion of TI is rarely if ever found normally (64). A decrease in voltage or reversal in polarity of the T wave in leads II and III during the change in position from the recumbent to the upright has been reported frequently in the literature. Scherf and Wiseberg estimated that 75 per cent of their 300 normal subjects showed a decrease in the height of the T wave in all limb leads during the change in posture from the recumbent to the upright (143). Sigler reported a diminished voltage, flattening or inversion of the T wave in either or both leads II and III under

similar conditions (147). Furthermore, it is known that transient variations in the T wave of leads II and III occur with those changes in posture (i.e. lying to upright) resulting in a right axis deviation (90, 126, 143, 168, 169, 182).

RS-T segment deviations occur normally in the standard leads in greater proportions than would be expected. It is reasonable to assume that since RS-T deviations are a normal occurrence, a slight displacement of the segment when it occurs during postural changes has no greater significance than the variations in the T waves observed under similar conditions.

In the Levy, Rothschild and Kissin anoxemia test and Master's two-step test, the positive electrocardiographic changes usually manifest themselves after a latent period varying from two to eight minutes. In these experiments positive changes occurred immediately upon tilting and thereafter progressed as long as the tilt position was maintained. It seems unlikely that in these circumstances anoxia sufficient to produce electrocardiographic changes could develop within a few seconds. The diminished amplitude and reversal in polarity of the T waves, therefore, must be ascribed to other causes.

If it is assumed that the T wave changes observed in cardiac patients and patients with Neurocirculatory Asthenia during tilting are due to anoxia, then it must also be assumed that most normal adults suffer equally from anoxia when they adopt the upright position as similar T wave changes are observed in their electrocardiograms during the 70 degree tilt or upright position. It is much more reasonable to assume that the reversal in polarity and decrease in amplitude of the T wave during the change from the dorsal recumbent to the upright is due to purely physiological reactions, such as the following: 1) Alteration of

the position of the heart in the chest. 2) Increase in the heart rate which, according to Ashman (4), abbreviates and equalizes the repolarization process of the cardiac musculature producing a condition similar to that observed in the primitive heart. 3) Influence of the sympathetic nervous system on the recovery cycle of the ventricles. It is known that sympathetic stimulation may alter the T waves (8) and is therefore plausible that the T wave might be influenced by the reflex sympathetic stimulation produced by the alteration in position, which finds expression in the increase in the heart rate.

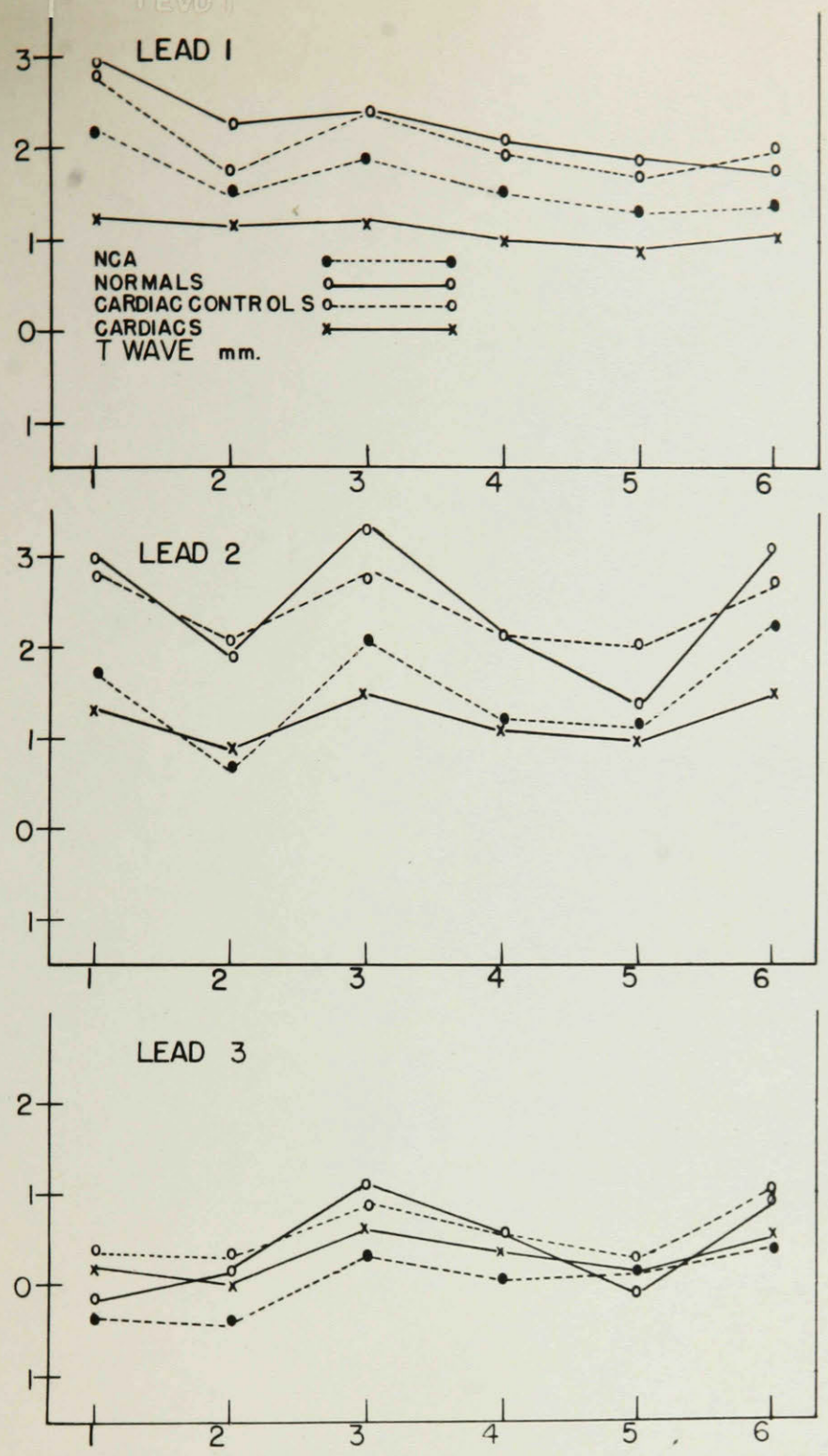


Fig.1- The average amplitude of the T wave in millimeters in the three conventional limb leads (ordinate) during: 1) sitting, 2) standing, 3) dorsal recumbent (initial), 4) immediate 70 degree tilt position 5.10 minute 70 degree tilt position, 6) dorsal recumbent (final).

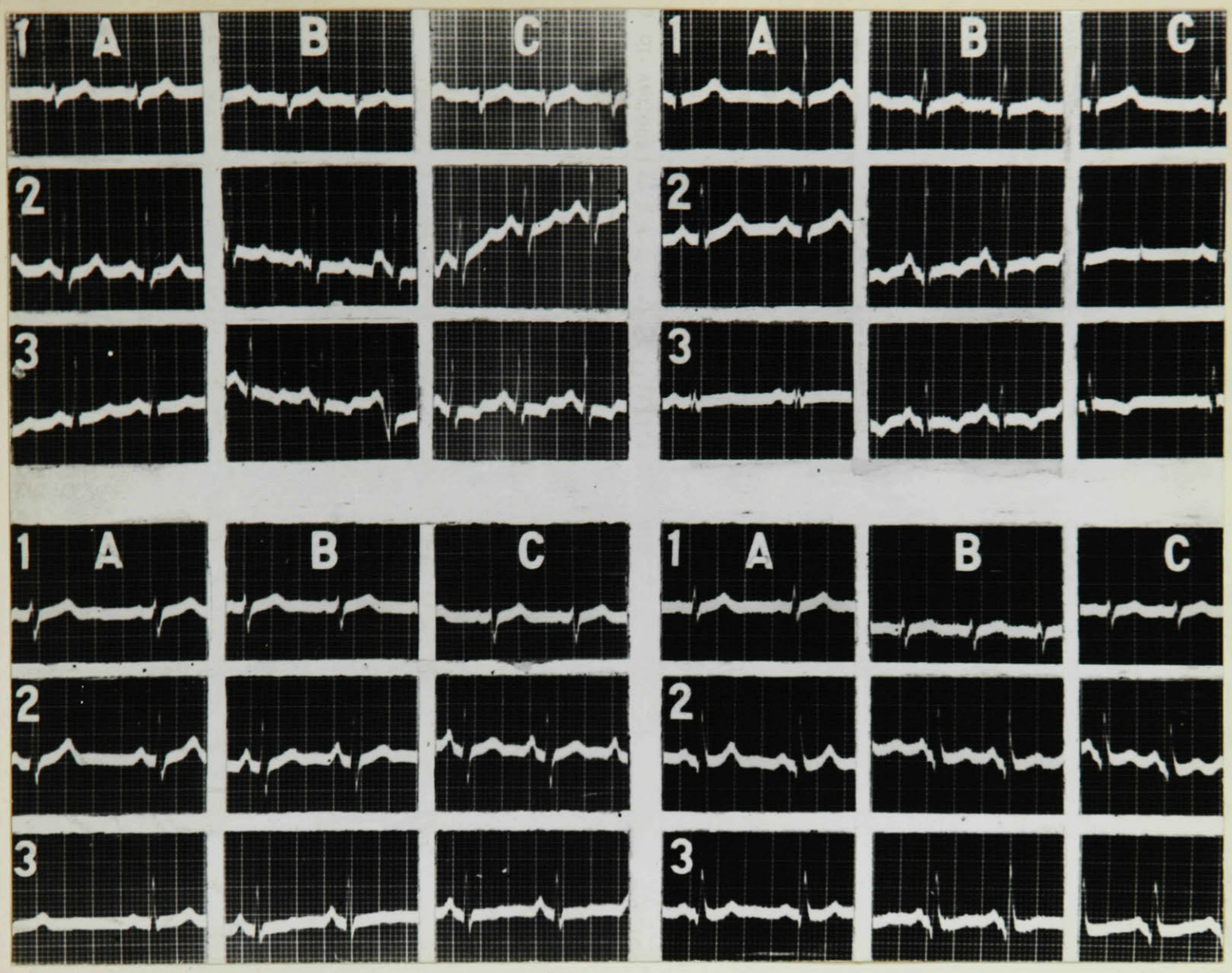


Fig. 2 - Four male subjects with Neurocirculatory Asthenia. Upper left C. F., age 26; lower left R.S., age 23; upper right G. P., age 22; lower right P. G., age 21. Numbers 1, 2 and 3 indicate the three conventional limb leads, letters A, B and C indicate the dorsal recumbent position, immediate 70 degree tilt position and 10 minute 70 degree tilt position respectively.

1. Upper left. A: T waves upright in all leads, rate - 108. B: T_1 unchanged; T_2 decreased in amplitude; T_3 inverted, rate - 125. C: T_1 and T_2 unchanged; T_3 inverted, rate - 125.

2. Lower left. A: T waves upright in all leads; U wave present in leads I and II, rate - 70. B: T_1 and T_2 decreased in amplitude; T_3 diphasic; U wave persists in leads I and II, rate - 92. C: T waves upright in leads I and II; T_3 diphasic, rate - 100.

3. Upper right. A: T_1 and T_2 upright; T_3 upright 0.5 mm.; U wave present in lead II; QRS_3 shallow, rate - 81. B: T_1 upright; T_2 and T_3 inverted; R_3 increased, rate - 100. C: T_1 increased in amplitude; T_2 upright; T_3 inverted; R_3 increased, rate - 71.

4. Lower right. A: T waves upright in all leads; S_1 shallow, rate - 83. B: T_1, T_2 and T_3 decreased in amplitude; S_1 deeper than S_1 in A, rate - 110. C: T_1 and T_2 unchanged from B; T_3 further decreased in amplitude; S_3 unchanged from B, rate - 125.

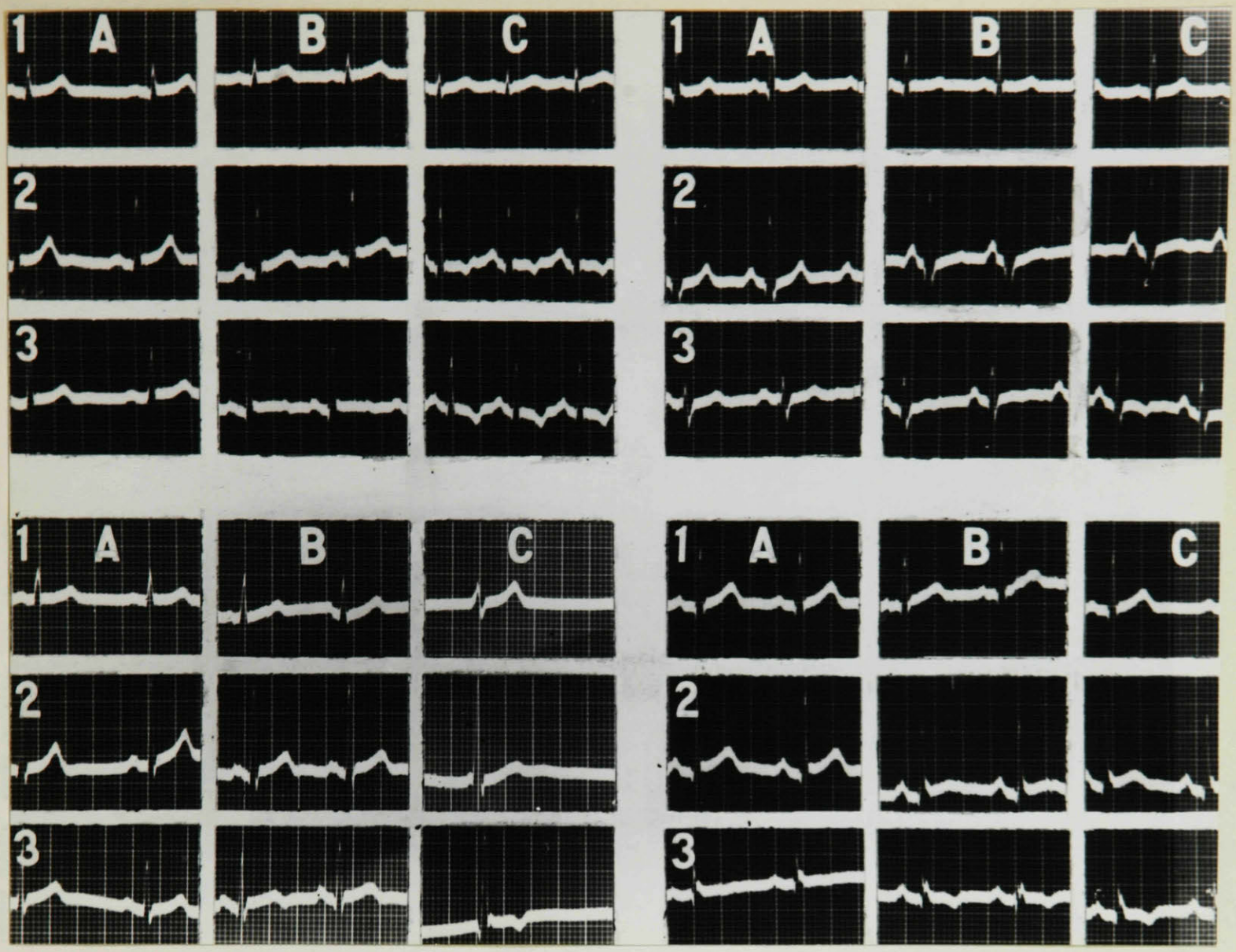


Fig. 3 - Four normal male controls, upper left F.D., age 26; lower left L. L., age 24; upper right L. A., age 28; lower right C. D., age 28. Numbers 1, 2 and 3 indicate the three conventional limb leads; letters A, B and C indicate the dorsal recumbent position, immediate 70 degree tilt position and 10 minute tilt 70 degree position respectively.

1. Upper left. A: upright T waves in all three leads. Note the physiological deviation in RS-T in all leads, rate - 68. B: amplitude in T_1 and T_2 is decreased. There is flattening with a tendency to a diphasic T in lead III. Note that RS-T_2 deviations have increased, rate - 100. C: T_1 unchanged; T_2 and T_3 are deeply inverted; RS-T_1 and RS-T_2 are now isoelectric, rate - 120.

2. Lower left. A: upright T waves in all leads, rate - 75. B: T_1 unchanged; T_2 decreased in amplitude; T_3 decreased in amplitude and tendency to diphasic, rate - 85. C: T_1 increased amplitude; T_2 decreased in amplitude, note the appearance of a U wave in lead II; T_3 inverted. Axis had changed from a normal axis towards a right axis, rate - 60. T_3 has inverted despite slowing in rate.

3. Upper right. A: All T waves are upright, rate - 86. B: T_1 and T_2 decreased in amplitude; T_3 inverted, rate - 93. C: T_1 upright; T_2 diphasic; T_3 inverted, rate - 100.

4. Lower right. A: T_1 and T_2 upright; T_3 flat; RS-T elevated in all leads, most pronounced in lead II, rate - 75. B: T_1 and T_2 decreased in amplitude; T_3 inverted; RS-T elevation unchanged, rate - 86. C: T_1 and T_2 unchanged; T_3 inverted; RS-T elevations unchanged, rate - 86.

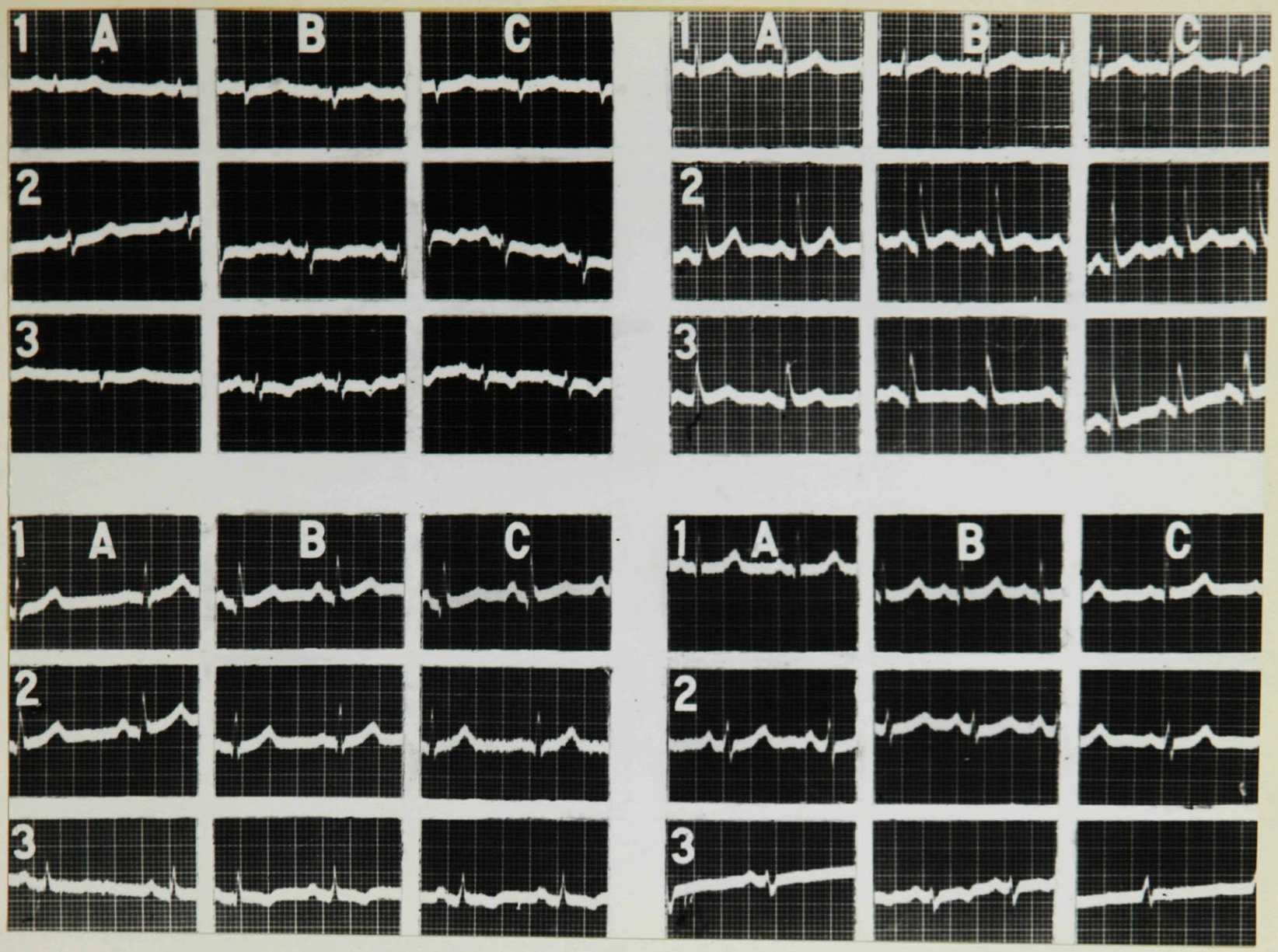


Fig. 4 - The upper two sets of records are those from cardiac patients. Upper left I. V. hypertension and angina of effort 38 (female). Upper right C. L. hypertension and angina pectoris 49. The two lower sets of records are those from cardiac control subjects. Lower left P. D. 47; lower right E. K. 38 (female). Numbers 1, 2 and 3 indicate the three conventional limb leads; letters A, B and C indicate the dorsal recumbent position, immediate 70 degree tilt position and 10 minute 70 degree tilt position respectively.

1. Upper left. A: T_1 and T_2 upright; T_3 upright but shallow, rate - 66. B: T_1 upright and unchanged, T_2 and T_3 inverted, rate - 90. C: T_1 upright; T_2 and T_3 inverted, rate - 107.

2. Upper right. A: T waves upright in all leads; RS-T elevated in lead II, rate - 91. B: T waves upright in leads I and II, but decreased in amplitude; T_3 inverted; RS-T elevated in lead II as in I, rate - 107. C: T_1 and T_2 upright, but decreased in amplitude; T_3 inverted, rate - 125.

3. Lower left. A: T_1 and T_2 upright, T_3 isoelectric, rate - 66. B: T_1 and T_2 upright; T_1 decreased in amplitude; T_3 inverted, rate - 81. C: T_1 further decreased in amplitude; T_2 unchanged; T_3 inverted as in B, rate - 83.

4. Lower right. A: T_1 and T_2 upright; T_3 isoelectric, rate - 83. B: T_1 and T_2 upright and virtually unchanged from A; T_3 inverted, rate - 96. C: T_1 and T_2 upright and unchanged from A or B; T_3 isoelectric with a semblance of inversion, rate - 92.

IV. THE PHYSIOLOGICAL BASIS OF THE SIGNS AND SYMPTOMS OF NEUROCIRCULATORY ASTHENIA.

The Harvard study (128) indicates that the symptoms of Neurocirculatory Asthenia are numerous and quite consistent in all typical cases. As the symptoms are not limited to the cardiovascular and respiratory systems, but include the nervous, gastrointestinal and locomotor systems, it has been suggested that Neurocirculatory Asthenia is a syndrome involving the body as a whole (64).

The following table lists the symptoms in their order of prevalence and compares the occurrence of like symptoms in normals with those in patients with Neurocirculatory Asthenia (128):

	50 Patients	55 Controls
Dyspnoea	100	13
Effort trouble	100	11
Attacks	98	4
Palpitations	98	15
Chest pain	92	7
Fear	92	0
Insomnia	92	20
Fatiguability	90	5
Nervousness	90	11
Apprehensiveness	90	2
Weakness	88	2
Gastrointestinal	87	40
Shakiness	85	13
Faintness	84	11
Sweating		24

	50 Patients	55 Controls
"No hard work"	83	0
"Easily upset"	80	77
Irritability	80	29
Breath unsatisfactory	79	2
Gas mask trouble	78	15
Throbbing	77	7
Weight loss	76	20
Trembling	73	15
Sighing	69	9
Unhappiness	68	15
Panting	66	5
Headache	66	13
Indigestion	64	25
Excessive self-observation	64	5
Nightmares	63	16
Anxiety attacks	60	2
Anorexia	56	15
Attacks of excitement	54	0
Syncope	43	13

A discussion of these symptoms follows:

1. Dyspnoea.

Dyspnoea is the consciousness of the necessity for increased respiratory effort (15). It may be initiated by sudden pain, exposure to cold, excitement, anger and physical or mental stimuli. The depth and rhythm of respiration may be so affected in neurotic and hysterical patients that dyspnoea appears to be present (30, 118).

Dyspnoea may begin as a result of emotional upset and persist to such a degree that the individual believes he has asthma (115).

Haldane and Douglas (44) showed that a decrease in carbon dioxide stimulates the respirations and simultaneously increases the sensitivity of the respiratory to carbon dioxide. As the respirations increase in vigor, carbon dioxide is washed out to a concentration below the amount required to stimulate the respiratory center. When this occurs, apnoea sets in. During the ensuing ten to fifteen seconds of apnoea, carbon dioxide accumulates again, stimulates the respiratory center and the cycle repeats itself.

There is no doubt that many patients with Neurocirculatory Asthenia do hyperventilate (148). Hyperventilation, according to the Haldane-Douglas theory, will produce minute periods of apnoea. The patient suffering from Neurocirculatory Asthenia prior to and during hyperventilation is probably in a state of increased emotion. When physiological apnoea sets in, his former emotional state is exaggerated because "he can't breathe"; when the period of apnoea wanes, hyperventilation again sets in. Eventually, a vicious circle is established.

At the present time there is no organic explanation for hyperventilation and breathlessness in individuals with Neurocirculatory Asthenia. Breathlessness is neither due to diminished vital capacity (1,101), nor to an accumulation of metabolites in the vicinity of the respiratory center (179).

It is known that hyperventilation and breathlessness may be initiated by sudden pain (141), excitement (52) and physical or mental stimuli (52, 58). Hyperventilation is frequently observed in individuals who are in poor physical condition during exercise.

Since there is no organic basis for these two symptoms, it is reasonable to assume that in these subjects, hyperventilation and breathlessness are both a hyper response to illusory dangers.

2. Effort trouble, fatiguability, shakiness and trembling.

These symptoms are listed together since they are usually found as a group.

"Fatigue may be defined as a progressive diminution in output resulting from the repeated performance of a given action" (80). Anyone acquainted with individuals who are out of physical condition is aware that such individuals tire more quickly than individuals in better physical condition. Fatigue and "effort trouble" in Neurocirculatory Asthenia are in part due to the patient's inexperience with hard work and exercise and in part due to their constant emotional conflicts. This hypothesis is borne out by the fact that when individuals suffering from Neurocirculatory Asthenia are brought into a secure environment, they gradually increase their work output by a special training program (103). In this respect patients with Neurocirculatory Asthenia behave like individuals in poor physical condition and recent convalescents (103).

Two of the most constant expressions of nervousness are shakiness and trembling. These two signs are often seen during or after spontaneous or experimental hyperventilation. In Neurocirculatory Asthenia shakiness and trembling are usually present at all times, but are exaggerated many fold during training for active combat (103). A plausible explanation for this phenomenon is as follows. The intensity of shakiness and trembling is due to the synergic effect of fear and hyperventilation.

During combat training, the patient with Neurocirculatory Asthenia hyperventilates more than usual because of his inexperience with exercise and because of his great fear of the actual combat for which he is preparing. Ordinarily, either hyperventilation or increased fear will produce a certain degree of shakiness and trembling, but when hyperventilation is added to the factor of fear, each intensifies the other, eventually establishing a vicious circle which further increases the degree of shakiness and trembling.

3. Headache.

Among the numerous causes of headache are worry, excitement, fear, anguish and other emotional states. Since patients with Neurocirculatory Asthenia are particularly prone to such conditions, it is reasonable to assume that the headaches in such subjects are for the main part produced by the above mentioned conditions.

The headache in Neurocirculatory Asthenia is usually localized to the front, back or top of the head. There is usually a feeling of a tight hand about the head or a heavy weight on the vertex. Neurasthenic individuals often give a similar description of their headaches which are "usually of psychogenic origin" (118).

Headaches are thought to arise from the dilation of the pial vessels and the larger vessels of the dura mater (15). The pial vessels are controlled mainly by the sympathetic nervous system. Stimulation of the sympathetic nervous system will cause vaso-constriction of the pial vessels and paralysis of the sympathetic nervous system produces vaso-relaxation of the pial vessels. Prolonged vasoconstriction will produce oedema in the pia matter which results in the feeling of "headache".

Hyperventilation is thought to stimulate the sympathetic

nervous system. If this be so, then the pial vessels could constrict and eventually the patient could experience a "headache". Headaches are often present in these patients after exercise. This may be due to hyperventilation which occurs during the period of compensatory breathing (180) to repay the oxygen debt incurred during the exercise.

4. Perspiration.

Patients with Neurocirculatory Asthenia perspire to such an extent that it is frequently a major complaint. The areas afflicted are the palms of the hands, the axillae and the brow. The perspiration is of the "cold" variety (103).

Psychic influences, such as nervousness, fear, fatigue or worry cause "cold sweat" to appear in the same locales (palms of the hands, axillae and the brow), as are commonly observed in Neurocirculatory Asthenia. The reflex center for this phenomenon may possibly be located in the hypothalamus for it is known (118) that lesions in the vicinity of the hypothalamus produce excessive perspiration. No one has yet reported any intracranial organic lesion in Neurocirculatory Asthenia so that we are reasonably certain that perspiration in Neurocirculatory Asthenia is due to causes other than organic intracranial expanding lesions.

The sweat glands are controlled by the sympathetic nervous system, but secretion is influenced only by parasympathometic drugs. Wood injected patients subcutaneously with 6 mgs. of acetyl-beta-methyl-choline (a powerful parasympathometic drug) and observed that patients did not perspire as much as did controls. The following table is a summary of his results.

Perspiration (continued)

Cases	Brow	Chest	Axilla	Free Palm	Obstructed Palm
15 patients	1.6[x]	1.2	0.8	0.3	0.6
5 controls	3.2	1.8	1.8	1.6	.40

[x]Wood's own units

From Wood's experiments it may be concluded that there is no hypersensitivity of the nervous control of the sweat glands in patients with Neurocirculatory Asthenia.

From the preceding paragraphs it is reasonable to assume that perspiration in Neurocirculatory Asthenia is mainly due to psychic influences, such as nervousness, fear, fatigue or worry.

5. Palpitation

Palpitation is the consciousness of the heart beat. It is due either to extra-systoles or to actual consciousness of the heart beating against the chest wall. In patients with Neurocirculatory Asthenia extra-systoles are probably as frequent as in the general population and no more. That extra-systoles may be the cause of palpitation in a few of these patients cannot be denied, but there is more likelihood that palpitation in the patient with Neurocirculatory Asthenia arises from other causes. It is probably a physiological reaction to fear. This contention is supported by the following quotation taken from Miller and McLean (122).

"Palpitation is biological manifestation of fear in the face of danger. The increased pulse rate and intensified heart action make the individual subjectively aware of the increased activity of the heart. Situations which produce palpitations involve an immediate urge to activity and at the same time a fear of it. Common examples are: palpitation experienced upon receiving a rebuke from one's superior, taking an examination, going to a forbidden amatory rendez-vous and the like. In all of these situations the individual is driven by his active, ambitious attitude into an apparent danger at the same time he feels an urge to avoid. His flight is blocked".

Lewis (103) believes that palpitation has no significance from a prognostic standpoint, other than the significance of a high pulse rate.

6. Syncope

Syncope may be defined as an acute and transient bodily state associated with sudden, partial or complete cessation of the circulation with loss of power of locomotion and loss of consciousness.

Syncope has been observed in 85% of all patients with Neurocirculatory Asthenia (128); this is a much higher figure than that calculated in the laboratory by the author and Best and that of Lewis' in which syncope was present in only 35% and 60% respectively. As a rule, syncope in soldiers occurs following venae punctures or the maintenance of an erect posture for an hour or two; but, spontaneous syncope is not uncommon (103).

Lewis termed the type of syncope observed in Neurocirculatory Asthenia as predominantly vasovagal. This view is now opposed by Spillane (149) and Wood (178).

Lewis maintained that patients with Neurocirculatory Asthenia have a hypersensitive carotid sinus, which,when stimulated by psychical or physical means, produced a fall in systemic blood pressure with resultant cerebral anemia and syncope. Both Spillane and Wood believe that the mechanism of syncope in Neurocirculatory Asthenia is unknown but that it"usually represents an emotional reaction" (178). They oppose Lewis on the grounds that they were unable to demonstrate a single "hypersensitive" carotid sinus in their patients suffering from Neurocirculatory Asthenia.

7. Tachycardia.

The term means quick heart. The normal heart rate in adults varies from 60-80 beats per minute.

The heart rate in patients with Neurocirculatory Asthenia varies from 100 - 120 beats per minute with abrupt fluctuations therefrom often as great as 20 to 30 beats per minute (33). The cause of tachycardia and the fluctuations therefrom is probably due to sympathetic stimulation during apprehension associated with the reflex cardiac mechanism to increase the cardiac output when there is a diminished venous return by increasing the number of beats per minute (169).

8. Increased blood pressure.

The normal blood pressure in adults varies from 110-135 mm mercury systolic and from 70-85 mm mercury diastolic. In patients with Neurocirculatory Asthenia it is commonly found that the blood pressure readings are 150 mm mercury systolic and 90 mm mercury diastolic. These readings will usually fall during bed rest to 130 mm mercury systolic and 80 mm mercury diastolic.

Blood pressure is extremely labile in normal well balanced individuals. Mild fluctuation occurs during eating, sleeping, smoking and excitement. Other than pathological changes, nervous tension influences blood pressure to the greatest degree. This is demonstrated during routine examinations of university students, army inductees or life insurance candidates (169).

Patients with Neurocirculatory Asthenia as a rule are more prone to nervous excitement than normal individuals. Taking this fact into consideration and the fact that nervous tension is a powerful factor in producing increased blood pressure, it is reasonable

to assume that nervous factors play a dominant role in the increased blood pressure which is usually observed in the patient with Neurocirculatory Asthenia, when the physician examines the patient for the first time. This increased blood pressure is not true hypertension as it tends to drop and remain at a normal level when the patient is kept in bed for a few days and then removed to more "pleasant surroundings".

The increased blood pressure in Neurocirculatory Asthenia is probably due to "nervous tension" as it disappears under conditions such as bedrest and "pleasant surroundings".

9. Size of the heart by teleoroentgenogram.

In keeping with their asthenic body builds and moderate nutritional inferiority (120), the hearts in patients with Neurocirculatory Asthenia are not enlarged (126). This observation was also made on children with a tendency to vasoneurosis (13). Meakins and Gunson (126) reported that the hearts in patients with Neurocirculatory Asthenia were on the average 0.7 cm smaller than in normals.

10. The Electrocardiogram.

Those who maintain that there is a definite electrocardiographic picture in Neurocirculatory Asthenia call attention to the inversion of T, T2 and T3 in the conventional limb leads (166). These changes cannot be taken as conclusive diagnostic signs for Neurocirculatory Asthenia due to the normal variability of the T wave (106, 164).

It was previously mentioned in this thesis, that there are two tests described by which the authors contend Neurocirculatory Asthenia may be differentiated from other types of cardiac disease.

The first or Bartlett tilt-table test has been considered at some length elsewhere and it is sufficient to say that this laboratory is unable to support the test. The second, or Wendkos test, has possibilities, but it requires repetition and corroboration before it can be accepted.

It is, therefore, reasonable to conclude that there is no positive electrocardiographic evidence of Neurocirculatory Asthenia.

11. Systolic Murmur.

A systolic murmur is sometimes heard in the pulmonic and mitral areas in Neurocirculatory Asthenia.

The systolic murmur heard in the pulmonic region waxes and wanes with expiration and inspiration respectively. It is soft and blowing and is best heard in the recumbent position.

The systolic murmur heard in the mitral area is usually soft and blowing, follows the first sound and is not transmitted. It is heard best in the recumbent position.

The above two described murmurs are considered to be physiological for the following reasons.

1. The systolic murmur of pulmonary disease, i.e. stenosis, is harsh and blowing and does not wax and wane during expiration and inspiration respectively. It is heard well no matter what position the patient assumes.

2. The systolic murmur of mitral disease, i.e. regurgitation, is soft and blowing and is transmitted over a wide area in the precordium towards the left axilla as far back as the mid scapular line. The murmur often replaces the first heart sound heard in the mitral area. Murmurs other than those described herein should be fully investigated as organic heart disease may be a factor

in their production.

12. Giddiness and Dizziness.

Giddiness and Dizziness are frequent post exercise complaints in patients with Neurocirculatory Asthenia. These two symptoms are thought to be caused by the post exercise hyperventilation observed in these patients.

Giddiness and Dizziness are due to relative cerebral anemia. While hyperventilation is possibly one of the most common causes of cerebral anemia in these patients, other causes, such as anemia, psychic trauma (with or without hyperventilation) and sudden drop in systemic blood pressure must be ruled out before any conclusion can be made.

13. Precordial Pain.

Many soldiers with Neurocirculatory Asthenia complain of a left precordial pain, ranging from an isolated pricking or needle-like prick under the left pectoral muscle to a severe lancinating pain radiating down the inner aspect of the left arm, forearm and palm, and radiating up to the left aspect of the head and neck.

The pain just described above could be local and/or referred from some other section of the body which is subserved by the same area in the spinal cord.

The location of the inframammary pain does not disclose the origin of the pain. The skin in the inframammary region is supplied by sensory fibres from T2, T3, T4, T5, T6 with a possibility of other efferent nerves from C_7. Accordingly, any abnormality in the spinal cord in the above vicinity would cause pain to be referred to the skin in the inframammary region (40). The muscles in the area are supplied by nerves arising from C_5, C_6, C_7, C_8 and T_1 (19). Any injury to the aforementioned

nerves or area of the cervical cord would produce pain which would be referred to the pectoral region. The afferent nerves of the heart, which probably mediate the sensation of pain, accompany the first five thoracic nerves and the three cardiac nerves.

There are five possible explanations for precordial pain.

1. Cardiac (111, 137, 169).

2. Nervous or imaginary pain (145).

3. Medical conditions, such as herpes zoster, mediastinal tumors (169).

4. Faulty function of muscles and ligaments involved in respiration (138).

5. Myalgia resulting from fatigue of the accessory muscles of respiration (21, 22, 169).

Thus, the precordial pain in Neurocirculatory Asthenia may be due to any one of the five causes listed above. True cardiac pain is of serious import and signifies organic cardiac disease. However, the precordial pain in Neurocirculatory Asthenia is not referred from the heart and great vessels. This contention is supported by the following.

1. The sensation of precordial pain in Neurocirculatory Asthenia is dissimilar from that of coronary occlusion or angina of effort. Anginal pain is short, stabbing and transient in nature. The pain of coronary thrombosis is usually severe, lancinating, persistent and with a state of shock as an usual accompaniment. The sensation of pain as described by patients with Neurocirculatory Asthenia may suggest either of these two pathological conditions, but the finer details, such as duration, type, location and electrocardiographic pattern, do not suggest the complete picture of either angina pectoris or coronary occlusion.

2. Patients with Neurocirculatory Asthenia do not generally have extra-systoles which are occasionally a cause of cardiac pain.

3. No one has demonstrated any specific pathological changes in a heart taken from a patient who had suffered from Neurocirculatory Asthenia.

Right- or left-sided inframammary pain of nervous origin does exist (144, 168). There is, however, despite this evidence, reason to believe that the sensation of inframammary pain experienced by patients with Neurocirculatory Asthenia is not of this type.

1. The character and behaviour of the pain is too constant to be imaginary.

2. Doctors who have suffered from precordial pain other than cardiac in origin, do attest to its presence (179).

3. The pain cannot be abolished by suggestion or anaesthetizing the skin in the pectoral region.

Precordial pain caused by Herpes Zoster and mediastinal tumors is rarely, if ever, encountered in Neurocirculatory Asthenia. For this reason, I feel they are not worthy of discussion.

Having disposed of the hypotheses that left- or right-sided inframammary pain in Neurocirculatory Asthenia is cardiac, imaginary or pathologic in origin, we are left with the two remaining possibilities, i.e. malfunction and myalgia of the respiratory and accessory respiratory muscles of respiration.

Kellgren (91) produced the sensation of pain in the pectoral region by injecting 3.0 cc. of hypertonic saline in the vicinity of C_5, T_1 and T_2.

He suggested that the localization and extent of the sensation of pain may suggest its origin. Fascia and tendon pain

are sharply localized, while muscle and joint pain are diffuse. Furthermore, when the sensation of pain is referred from some muscular or ligamentous lesion, it is not relieved by skin anaesthesia (91).

The severity of the precordial pain in patients with Neurocirculatory Asthenia is not influenced by cutaneous or subcutaneous novocaine injections. Deep intramuscular injections abolish the sensation of pain, but the precordial skin is still sensitive to light touch and pin pricks. This experiment suggests that the precordial pain in Neurocirculatory Asthenia is localized to the muscle or ligaments and is not of the referred type.

The muscles beneath the skin in the precordial area are as follows: pectorals, intercostals, traingularis sterni and the insertions of the scalenius anterior, posterior and medius. Obviously the sensation of pain is caused by some disturbance in one or more of the above groups of muscles.

During a course of investigation of the origin of cardiac pain, Wood (178) fluoroscoped the movements of the diaphragm in numerous patients and picked out fourteen individuals in whom there were good diaphragm excursions, and fourteen in whom there were poor diaphragm excursions. In the former group, four of the patients complained of precordial pain, while in the latter group, all the patients complained of precordial pain.

Briscoe (21, 22) revived the theory that inframammary pain was caused by the lack of diaphragmatic breathing which caused excessive contraction and relaxation of the respiratory and accessory respiratory muscles. Wood (178) correlated the sensation of pain with the degree of diaphragmatic movement and thoracic excursion. The following table summarized his results:

	Number of Cases	Significant Pain	Pain trivial or absent
Relatively good breathers, diaphragmatic movement 7.5 cm. Lower thoracic expansion 7.3 cm. Upper thoracic expansion 7.25 cm.	40	12.5	87.5
Bad phrenic movement 4 cm. or less (normal thoracic expansion)	25	72	28
Bad phrenic and bad costal movement	10	90	10

Capps (28) asserted that the precordial pain is bilateral and is due to anoxia of the diaphragm, rather than irritation of the accessory respiratory muscles, as believed by Wood. Wood (178) knew that his hypothesis does not explain left-sided precordial pain. To qualify his hypothesis, he suggested that the patients consider palpitation and the left-sided pain as one entity. This confusion is generally strengthened by the persistence of the element of fear in these individuals.

In conclusion it may be said that inframammary pain in Neurocirculatory Asthenia patients is due to the following physical reasons superimposed upon an inherent psychological weakness.

1. Tendency to quick and shallow breathing, thereby using the thoracic and accessory respiratory muscles to excess.

2. Sudden stress and strain upon the respiratory and adjoining muscles during exercise in physically inferior individuals or individuals in poor physical condition.

3. Anoxia of the diaphragm.

4. Wood's theory of subconscious "splinting" of accessory respiratory muscles.

V. SUMMARY

1. Neurocirculatory Asthenia is a state of ill health characterized by a group of symptoms consisting of dyspnoea, effort trouble, palpitations, precordial pain, exhaustion, dizziness, nervousness and sometimes tremor, perspiration, headache and syncope. These symptoms are all aggravated by effort or excitement.
2. The concept of Neurocirculatory Asthenia has gradually changed from that of a purely organic disease of the heart with demonstrable pathological changes to that of a disorder of the whole personality without any evidence of heart disease.
3. Hard physical work, excess of tobacco and alcohol, pressure from clothing or infections, do not cause Neurocirculatory Asthenia.
4. Neurocirculatory Asthenia is more prevalent in men during wartime and in women during peacetime.
5. Neurocirculatory Asthenia occurs most frequently between the second and third decade.
6. Hyperactivity of the thyroid and adrenal (medullae) glands are not the cause of Neurocirculatory Asthenia despite the presence of symptoms such as tachycardia, increased blood pressure, perspiration and increased respirations which may be the result of excess secretion of these glands.
7. Hyperventilation may cause some of the lesser symptoms of Neurocirculatory Asthenia such as dizziness, headache, tingling and nausea, but is not the major factor responsible for Neurocirculatory Asthenia.
8. The personality of a patient with Neurocirculatory Asthenia parallels more closely the personality of a psychoneurotic

individual than it does a normal individual. This fact is borne out by the Rorschach test and the Minnesota multiphasic personality inventory.

9. Two psychic characteristics which are nearly always present in the patient with Neurocirculatory Asthenia are: a) "tendency to limit performance"; b) "give up easily in face of emotional difficulties".
10. There is a decrease in the apnoea time of patients with Neurocirculatory Asthenia as compared with normal individuals.
11. The vital capacity is not diminished in patients with Neurocirculatory Asthenia.
12. These patients do not score as well as normal individuals on functional efficiency tests of the cardiovascular system, such as the Meakins and Gunson test, the Harvard step test and the Johnson, Brouha and Darling test.
13. The sleeping pulses of patients with Neurocirculatory Asthenia and normal individuals are equal.
14. The circulation time and cardiac output in these patients are not increased.
15. There is neither impairment in lactic acid metabolism in the hearts of patients with Neurocirculatory Asthenia, nor is there an abnormal accumulation of lactic acid in the blood stream to alter the blood pH significantly.
16. There are no electrocardiographic criteria diagnostic of Neurocirculatory Asthenia.
17. A specific clinical test for Neurocirculatory Asthenia is lacking. The Bartlett tilt table test has been refuted by work done in this laboratory.
18. Hyperventilation and breathlessness are probably due to a hyper response of the patient with Neurocirculatory Asthenia to illusory dangers.

19. Effort trouble, fatiguability, shakiness and trembling may be due to excess hyperventilation superimposed upon an element of fear.
20. The headaches in Neurocirculatory Asthenia are probably the result of hyperventilation.
21. Perspiration in Neurocirculatory Asthenia is mainly due to psychic influences such as nervousness, fear, fatigue or worry.
22. Palpitation, syncope and increased blood pressure is probably a physiological response to fear in these patients.
23. The heart in Neurocirculatory Asthenia is not increased in size.
24. Precordial pain in Neurocirculatory Asthenia is not caused by disease in the heart tissues. Precordial pain is the result of any one of the following four physical factors.
    1. Tendency to quick and shallow breathing, thereby using the thoracic and accessory respiratory muscles to excess.
    2. Sudden stress and strain upon the respiratory and adjoining muscles during exercises in physically inferior individuals, or individuals in poor physical condition.
    3. Anoxia of the diaphragm.
    4. Wood's theory of subconscious splinting of the accessory respiratory muscles.

VI. CONCLUSIONS

1. Neurocirculatory Asthenia is a syndrome characterized by numerous symptoms of which dyspnoea, effort trouble and palpitation are the most prominent and frequent. These symptoms are aggravated by effort or excitement.
2. Neurocirculatory Asthenia is a disorder of the individual's total personality which is produced mainly by a discharge of excess nervous energy in individuals who are "constitutional inferior". The nervous energy is produced during fear. Instead of normally being able to express the emotion at the conscious or behavioral level, it is partially repressed and only lower level visceral smooth muscle activities mediated by the sympathetic nervous system are manifested. These latter consist of palpitation, perspiration, tremor, increased heart rate, vomiting and diarrhoea.
3. There is no organic cardiac disease in patients suffering from Neurocirculatory Asthenia.
4. The hyperventilation theory of Soley and Shock, which ascribes the symptoms and signs of Neurocirculatory Asthenia to constant hyperventilation in these patients, cannot be supported on the basis of the results obtained in this laboratory.
5. The reversal in polarity or decrease in amplitude of the T waves during the change in position from the dorsal recumbent to the 70 degree tilt position is a physiological response which young adults manifest to a greater degree than the other adults, and which normal subjects show to as great or greater extent as patients with Neurocirculatory Asthenia or coronary artery disease. The electrocardiographic changes

that transpire in the tilt table test cannot therefore be utilized to distinguish between normal individuals, those with coronary artery disease and those with Neurocirculatory Asthenia.

6. The cardiac symptoms in Neurocirculatory Asthenia are not due to the accumulation of lactic acid in the blood for the amount of lactic acid accumulated in the blood in these patients is insignificant to the amount which is necessary to produce any alteration in the cardiac mechanism.
7. There appears to be little if any difference in the physiological state of patients with Neurocirculatory Asthenia as compared with normal subjects. This is borne out by the evidence accumulated in this laboratory by comparing the response of patients with Neurocirculatory Asthenia and normal subjects to various physiological tests.

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