1937

Arterial hypotension

Floyd L. Woolcott Jr.
University of Nebraska Medical Center

TABLE OF CONTENTS

I N T R O D U C T I O N

In discussing the finding, hypotension, it will be the intent of the author to determine its importance in the medical field. Low blood pressure has been reported in the literature associated with clinical and experimental shock since the year 1839 and yet, until recent years, the part that it plays in the individual's constitutional background has been neglected. Garvin(57), in 1927, is quoted as saying, "Comparatively few have been the communications in the various journals on the subject of low blood pressure. As opposed to hypertension, it pales into insignificance in the niche which it occupies in medical literature".

I have attempted to present a very comprehensive resume' of the literature as regards etiology of hypotension, with the exception of the condition known as Addison's disease, which, due to its scope, would be too great a task to present in this paper. The chapters on etiology, pathology, and treatment will be presented in a chronological manner in an effort to point out the views as they have appeared in the literature.

It is the hope of the author that the following pages will make the clinical observer a little more conscious of the condition of hypotension as it presents itself, and that a more careful study will be instituted as to its real significance.

D E F I N I T I O N

Hypotension is a condition characterized by a systolic blood pressure of below normal for the individual concerned, and manifest by certain symptoms, pathology, et cetera, discussed in the body of this paper. It has been described by many authors through the literature, and various terms have been used by them to convey its meaning. Ferrannini(49) reported that Martinet, in 1918, used the word "hyposphyxy" synonymomously, and in the same year, Vincent referred to hypotension as the "particular symptomatic triad". In 1927, Weiss wrote of a case of "arterial hypotony" in which the symptoms were identical to those that have later been described as present in hypotension. The word itself, however, strictly means "lessened tension", the tension referred to, of course, being that of the arterial wall of the blood vascular system.

Quoting Levison(78), in 1924, "--It seems eminently proper to use the expression arterial hypotension in designating a state of blood pressure lower than the normal expected for that individual person. ------I think that it may be said that increasing familiarity with the variability of blood pressure readings tends to lower the level at which one considers hypotension to be a clinical factor in disease". In view of this statment of Levison and the fact that other writers have expressed the same opinion, the author will not attempt to place a level, in millimeters of mercury, at which arterial pressure may assume the

title of hypotension, and from hereon will assume it to be a relative condition.

The condition of orthostatic hypotension referred to in this paper is a condition in which the blood pressure decreases only when the posture of the individual is changed from one of recumbency to one of standing. Many authors, in writing of this particular phase of hypotension, call the condition "postural hypotension". Allen and Magee(4), however, point out that the term "postural" is inadequate--that it does not explain the situation, whereas "orthostatic" refers to "pertaining to or caused by standing erect". It seems to me that this reference to terminology should be borne in mind and in the contents of this report, I have followed the plan of Allen and Magee and used "orthostatic" rather than "postural".

E T I O L O G Y

The first references found in the literature regarding low blood pressure were experiments carried out on dogs in 1839 by Blake(18). The normal blood pressure of these animals was determined by inserting a haemodynamometer into the femoral artery and observing the height to which the mercury rose; this was found to be at a level of six and one-half inches. The first experiment was one in which the animal was not allowed to breathe. At the very onset the mercury fell to a level of three and one-half inches and remained there for a period of two minutes, and during this time the heart pulsations became much slower. The lungs were then reinflated and the mercury rose to its previous level of six and one-half inches, in twenty-five seconds.Blake(18) next removed eighteen ounces of blood from the vein of the test animal and observed that the pressure dropped markedly. He then injected a solution of potassium nitrate, fifteen grains to six drams of water, into one of the test dogs. In ten seconds the blood pressure began to drop and in thirty seconds it had fallen to a level of one and one-half inches of mercury, and in forty-five seconds the animal was dead. Into another dog, he injected six drams of a concentrated infusion of gall, and found that the heart stopped beating in fifteen seconds. In a few more seconds the blood pressure began to fall and in a few minutes the animal was dead. He then injected an infusion of ten grains of tobacco into another of his animals. At the beginning of the injection,

the mercury stood at a level of four and one-half inches, but fifteen seconds later it had dropped to two inches--the heart stopped beating for several seconds and then again resumed its beat. The mercury then rose to six and then to twelve inches before levelling off. By injecting euphorbium into another test animal, results which were identical to those observed in the preceding experiment were obtained. Blake(18) then injected one dram of an infusion of digitalis into one of the dogs and found that the blood pressure dropped from a level of five inches of mercury to one of two inches in fifteen seconds but in just a few seconds the heart began to beat stronger and a compensatory rise occured which carried the level to eight inches. In his last experiment, he injected morphine and noted the blood pressure dropped only slightly. All of Blake's(18) experiments were carried out under exactly controlled conditions and were found to vary but little with other tests in which the blood pressure was lowered experimentally.

Traube(85), in 1864, was the next to report observations on lowered blood pressure. In that year, he injected a thirty three percent solution of sodium cholate into the vein of a dog and noted that there was a considerable drop in the blood pressure. About twenty years later, Loewit(85), in 1864, also experimented with sodium cholate and its effect on the blood pressure. He, however, used much weaker strengths of the substance but noted the same effects on the blood pressure, although they were not so marked. No other work was reported then, until 1891 when Heiden-

hain(55) discovered, rather accidentally, that the blood pressure dropped quite noticeably when peptone was injected into the circulation.

Cyon(73) was of the opinion that the blood pressure would rise if the cerebral hemispheres were intact, and that it would fall if the hemispheres were not in continuity. Dittman(73), however, showed that the pressure would rise even after severance of the hemispheres, thus disproving the contention of Cyon(73).

In 1894, Howell(73) cooled a portion of the sciatic nerve to zero degrees centigrade and then stimulated the nerve peripheral to the point of cooling. He noted, from this experiment, that there was a reflex fall in the blood pressure. He thus concluded that there were present both pressor and depressor fibers, but that the latter did not lose their power of conducting impulses at a low temperature as readily as the former.

In the same year, Hunt(73) reported that there were also fibers which affected the vasomotor center and caused a fall in the blood pressure, and that these were supposed to come from the heart. He, also, concluded that when mixed nerves were stimulated, the drop in blood pressure was due probably to a reflex stimulation of the dilator fibers, and that by stimulating the central end of sensory nerves there follows a reflex constriction of some arteries, causing a rise in the blood pressure and a reflex dilatation of other arteries, causing a drop in the pressure.

Latschenberger and Deakna(73), in the following year, were

the first to investigate the effect of stimulation of the afferent nerves on the blood pressure. They determined that a fall followed long continual stimulation of the sciatic nerve trunk. They found further, "that when the pressure in one vascular area was decreased (e.g. by clamping the artery) the pressor fibers were stimulated and a rise occurred, whereas, when the pressure was suddently increased (e.g. as when the clamp was removed) the depressor fibers were stimulated and a fall in the arterial pressure resulted". They concluded that depressor,as well as pressor, fibers ran from all of the blood vessels to the vasomotor center. Other writers, at about this same time, thought that the fall was due to altered conditions of the vasomotor center, however, they probably failed to find the depressor fibers.

Choline was discovered in 1862 by Strecker and in 1899, Halliburton and Mott(70) observed that it caused the arterial pressure to fall. The substance itself is an organic base derived from trimethylamine and was thought by Strecker to be generated in the body and to act by depressing the vasomotor system.

From 1899 until 1905, no additional findings were made as to the possible etiological factors causing low blood pressure, but in 1905, Meltzer and Salant(86) discovered that the blood pressure would drop, following the injection of whole bile. They used experimental dogs for their work and noted that the blood pressure would fall and then death would ensue.

In the following chart is a summary of the work that they

accomplished:

INJECTED	TIME	RESULTS
2.5 c.c. 10% ox bile	4 seconds	Death in 2 minutes
4.5 c.c. pure ox bile	30 seconds	Death in 3 minutes
5.0 c.c. pure ox bile	4 minutes	Gradual fall in blood pressure
2.5 c.c. pure ox bile	40 seconds	Slow fall in blood pressure
5.0 c.c. pure ox bile	3 minutes	Very slow fall in blood pressure
1.0 c.c. 2% ox bile	10 seconds	Fall of 12 m.m.Hg.

They concluded, from the above results, that the drop in the pressure depends on the toxic effect rendered, and that the toxic effect depends on the rapidity of injection and the concentration of the substance used. They also were of the opinion that the action was directed upon the myocardium itself.

In the same year, Hasselbalch(76) of the Finnish Institute, showed that irradiation with a carbon arc, using 150 amperes and 65 volts, lowered the systolic blood pressure of a normal person from eight to ten percent.

In 1908, Desgrez and Chevalier(70) stated that the fall in blood pressure was due to vasomotor dilatation of the vessels of the intestinal area. They, also, were the first to theorize that the effect of choline, the substance Strecker discovered, was one of neutralizing adrenalin, thus causing the lowered arterial tension. Modrakowsky(70), in the same year, and Busquett and Pachon (70) in 1909, made pure synthetic choline, and this pure product lacked all of the depressant powers of the preceding samples of the drug. They came to the conclusion, therefore, that the de-

pression must be due to decomposition products of choline, such as muscarine or neurine, rather than the choline itself. While Busquett and Pachon(70) were synthesizing choline, King and Stewart,(85) having read of the work of Meltzer and Salant(86), experimented with the effects of bile upon the vasomotor system. They observed that one minute following the injection of 5 c.c. of pure bile the blood pressure dropped from 120 to 50 m.m.Hg. It had been noted previously that bradycardia nearly always accompanied a fall in the blood pressure, but these men were of the opinion that the blood pressure fell first and that the bradycardia followed. Along with their work on bile, they tried two other substances, sodium glycocholate and sodium taurocholate, but observed no effect on the pressure after the use of either one of these.

In 1910, Musgrave and Sison(115) made the observation that the blood pressure of foreigners tended to become lower after being in the Philippines for ten years or longer. They thought that the climate, therefore, might act as an etiological agent in producing low blood pressure. It is true that there is increased sweating in the tropics but there is no definite knowledge of the relation of sweating to vasomotor states. It is also known that there is a cutaneous dilatation associated with sweating--also pallor with sweating, and sweating with fright. From these known factors hypotension cannot be explained on the basis of sweating, that is, assuming the hotter climate to be

the supposed etiological factor. Pearce and Eisenbrey(95), also in 1910, arrived at the same conclusion as did Heidenhain nineteen years before, that the injection of peptone would cause the blood pressure to fall in marked degrees.

In the following year, 1911, Edgecombe (48) listed several conditions in which a lowered arterial pressure was found. He stated first that persons with a poor circulatory mechanism were subject to hypotension. Several cases of neurasthenia were presented in which he considered that to be the causative factor. He thought, too, that gouty or rheumatic manifestations of lumbago, sciatica, and neuritis played some part in the altered mechanism of arterial tone, as likewise did rheumatoid arthritis. Lastly, he found that phosphaturia was nearly always accompanied by low blood pressure.

In 1914, the reflex theory was again brought forth, when Martin and Stiles(81) stated that the etiology could be based on this factor. They postulated that the hypotension may be the result of reduced tonic activity of the vasoconstrictor center, and if this were the case, the afferent fibers would have a depressor effect. They also mentioned that it may be due to the dilators, in which case the fibers would be called excito-dilators. He concluded, much the same as did Hunt(73), that, "the depressor nerve, or the depressor fibers, have been believed to effect a lowering of arterial tension partly through reflex inhibition of the heart, but more extensively, in the animals usually chosen for experiment,

by suppressing the tonic action of the vasoconstrictor center". Mann(21), in the same year, stated that the easiest and most certain method of producing shock is by exposure and traumatization of the abdominal viscera. This, judging from the literature, has been the method used by nearly all investigators of shock, and always produces a lowered blood pressure.

Wheelon and Shipley(59), in the following year, doing experimental work with dogs, discovered that following castration therewas first about a fifty percent decrease in the vasomotor response to nicotine, and second, that there was a marked fall in the systolic blood pressure. After noting these findings, they implanted testicular grafts and observed a twenty percent increase in the blood pressure. From these facts, they concluded that gonorrhea, causing testicular degeneration may be an etiological factor of lowered blood pressure in some instances.

Potter(102), in 1915, stated that the constant use of tobacco in large quantities predisposes to hypotension. He, also, recognized the well known fact, however, that the immediate effect of tobacco is to raise the blood pressure.

Simonds(110), in the next year, was of the opinion that low blood pressure due to hemorrhage and circulatory shock were identical in mechanism, in that in both, the venous supply to the right heart is the critical factor. However, he said that in circulatory shock there is a large reservoir of blood in the splanchnic area and in the liver, while in hemorrhage this con-

dition does not exist.

In 1916, Lawrence(77), reported that low blood pressure was present in cases of anemia, acute infections, debilitating diseases, and neurasthenia. He, also, was of the opinion that functional hypoadrenia caused lowered arterial tension. In the same year, Bayliss(14) in London presented two etiological factors--acute blood loss, and vasodilatation of the peripheral vessels.

In the following year, Pike and Coombs(101), reported a case in the literature of section of the spinal cord in the upper thoracic segment. They noted that in this case there was an associated drop in the arterial pressure and they attributed this fall to the traumatic injury. Also, in 1917, Simonds(111) of Chicago observed that after injection of a fat embolus and a solution of peptone into the vein of an experimental animal, a condition that resembled that of surgical shock in man resulted. He stated that the drop in the pressure followed only thirty seconds after injection of the peptone. The injection of the fat required several minutes to activate the fall that was comparable to that caused by the peptone solution.

Two years later, Dearborn(40), after reading about arterial hypotension, ventured his opinion that it was quite certain that at least a part of the lowness of the arterial tension was in reality the lowness of the tension of the muscles on which the syphygmomanometer cuff rested. He based his opinion on the fact

that muscle, fat and connective tissue are far from being the "ideal fluids" that the cuff-method theory demands.

In 1920, Dr. Thomas McCrae presented, in one of his clinics, his conception as to the etiological factors concerned in producing low blood pressure. He stated that the myocardium, arteries, capillaries, and the blood should all be considered as possibilities. He proved that he had seen cases of lowered pressure in which the heart wall itself had been pathological. The pathological processes present had varied from fatty degeneration to that of an acute myocarditis. He, also, stated that in cases of chronic aortitis the blood pressure was usually low. Although he gave no proof regarding the effect the capillaries might have played, he indicated that they may have been the seat of the pathology. The evidence that he presents that points toward the veins is that they may hold a large amount of blood, and thus keep it from reaching the heart. Or, the blood itself may be the causative agent, depending upon its quantity and quality. If there is an abnormal diminution of blood there will be a marked drop in the arterial pressure, and if the viscosity is lowered by saline injections or other intravenous medicaments the pressure will also diminish. If the carbon dioxide combining power is decreased sufficiently to cause an acidosis there will be a relative relaxation of the cardiac and arterial musculature with a resultant slowing of the circulation in the capillaries, causing a decrease in the blood pressure. Finally, McCrae(79)

sufficiency, loss of blood, and dilatation of the arterial vessels due to a paralysis of kinetic function or hypotonia of the muscles were three possible causes of low arterial tension.

Aldersberg and Tauerhause(85) experimenting with the same substances as did King and Stewart, namely sodium glycocholate, sodium taurocholate, and sodium dihydrocholic acid, found as they did, that none of the three compounds had any effect on the vasomotor status, causing the blood pressure to drop.

Garvin(57), in 1927, came to the same conclusion as did Martinet(70) six years before, and stated that he thought that the etiological factor involved in producing hypotension was hereditary, at least, in part.

In 1929, Houghton(68) organized a very thorough classification of causes of arterial hypotension. Although I am presenting the etiological history of hypotension in a chronological manner, I do feel that this outline should be presented because of its comprehensive scope.

I Causes due to failure of cardiac output:
  A. Intermittent cessation of beat--Stokes-Adams syndrome with bradycardia(heart block).
  B. Impulse weakness.
    1. Myocardial degeneration and dilatation secondary thereto.
    2. Valvular lesions, especially mitral stenosis and secondary auricullar fibrillation and aortic insufficiency.
    3. Aneurysm with hypotension distal to lesion.
  C. Postural hypotension.

II Causes due to diminution of blood volume or to morphological changes:
  A. Excessive hemorrhage, acute or chronic

B.Excessive loss of body water.
1.Persisting vomiting.
2.Persisting diarrhea(cholera asiatica).
C.Starvation and diseases leading to malnutrition.
D.Anemias
1.Polycythemia.
2.Pernicious and secondary anemias(cancerous cachexia), including other blood dyscrasias.

III Causes due to lack of vasomotor tonus:
A.Diseases of the cerebrospinal system(paresis, etc.).
B.Toxins of chemical origin.
1.Chloroform.
2.Spinal cord anesthesia.
3.Chloral hydrate, codeine, etc.
4.Early stages of lead poisoning.
5.Anaphylaxis produced by any foreign protein: especially including bacterial proteins.
C.Bacterial toxins, accompanied by changes in mineral-base concentrations in the blood plasma.
1.Specific infections.
a.Congenital and acquired syphilis.
b.Early stages of acute lobar pneumonia.
c.Influenza.
d.Typhoid fever.
e.Diphtheria.
f.Adrenal, pulmonary, and other tuberculosis.
g.Enterogenic intoxications.
2.Non-specific infections, especially residual streptococci and influenzal infection.
D.Endocrine dyscrasias.
1.Pituitary.
2.Adrenal insufficiency.

From the above outline, it can be readily noted that the four factors involved in the cause of hypotension are; first, failure of cardiac output; second, diminution of blood volume or morphological changes in the blood itself; third, lack of vasomotor tonus; and lastly, endocrine disorders. These findings seem to be confirmations of work that previous writers have accomplished, and agree in the greater part, at least, with those that have been presented to date in this paper.

Again, in 1929, we find Dumitresco and Mante(85) trying to

produce a fall in the blood pressure by using sodium glycocholate and sodium taurocholate, but to no avail. They concluded, as did their predecessors, that these substances had no effect on the blood pressure.

In 1930, Jones(117) noted that the blood pressure would fall following the administration of a spinal anesthesia. He explained the collapse of the vasomotor control by the absorption of the anesthetic drug into the general circulation. However, the absorption from the cerebrospinal fluid to the blood is very slow, and for this reason Jones' theory is not so very plausible. It seems more reasonable to assume that the marked drop in the pressure follows the generalized flaccid muscle paralysis and the paralysis of the sympathetic nerves.

In the same year, Vaughan and Graham(116), in checking cases of hypotension in the south, theorized that in hot humid climates where heat is not satisfactorily dissipated by perspiration, that the body accomodates by decreasing its adrenalin secretion. This reduction in the adrenalin output leads to vascular or circulatory asthenia and hypotension, with diminished sympathetic tonus in the gastrointestinal tract. In the same year, they reported that Friedlander was experimenting with dogs and found that the absorption of histamine caused the blood pressure to fall, and at the same time, Mosenthal and Greaves(64) were of the opinion that lowered tension was caused by the splanchnic pooling of blood.

Blalock(19), confirming the work of Friedlander, did experi-

mental work on dogs using barbital anesthesia and found that the blood pressure could not be reduced to shock levels by trauma to one of the posterior extremities, but that after histamine injections and massage to the limbs, the pressure did fall considerably.

Sanders(107), in the following year, reported a case history of a young man, twenty one years of age, who felt something "break" in his abdomen, while running. He appeared for an examination and it was found that his blood pressure was below the normal for his age and sex. Sanders said that it seemed reasonable to assume that a lesion in the autonomic nervous system was incurred at that particular time and that it was the cause of his hypotension.

In 1931, Blalock(21) did more experimental work on dogs. This time he traumatized their extremities and noted a marked drop in the systolic blood pressure. After determining the difference in the weight of the injured and the non-injured members, he noted that in all instances, it amounted to more than four percent of the total weight of the animal. After bleeding another dog four percent of its body weight during a similar period of time, the blood pressure also fell, thus the blood loss into the injured limb was believed to be responsible for the fall in the blood pressure. He concluded, therefore, that the loss of fluid into the traumatized region was the chief, if not the sole, cause for the reduction in the blood pressure. In doing further work on dogs with extensive burns, Blalock decided that he could not blame the loss of fluid alone for the drop in the pressure for

the toxic effect produced by the burn itself would be of some import. In doing additional work on experimental animals, he traumatized the intestinal tract and found that the loss of fluids from and into the traumatized tissues was again the chief, if not the sole, reason for the reduction in the blood pressure. Prolonged trauma to the intestinal tract resulted in a decline in the pressure due to a diminution in the circulatory blood volume, as a preponderance of evidence at that time indicated that there was a vasoconstriction,at least, during the early stages of shock.

In the same year, Ferrannini(49) stated that the morbid picture originated from abnormal constitutional conditions, depending on intoxications and infections that have acted in utero or during the first few years of life. He was of the opinion that these exerted a secondary influence on the organs regulating the development of the body generally, and of the vascular tissue in particular, especially of the adrenals, pituitary, and thyroid.

Meakin,(85) in 1932, is quoted, "It has long been known that obstructive jaundice produces circulatory disturbances and many attempts have been made to study them either by injecting bile or bile salts into animals. The principle attention has been directed to the bradycardia, the change in blood pressure being usually considered as a concomitant phenomenon, little attention being paid to it."

However, in scanning the literature since 1905, there have been several illuminating articles on the effects of bile on the circulatory mechanism, and most of them seem to point to the resultant drop in the blood pressure, rather than to the bradycardia that Meakin emphasizes. In the same year, Sanders(108) was of the opinion that the cerebral and cerebellar anemia that accompanies hypotension is responsible for the physical and psychical symptoms.

In 1933, Roome, Keith and Phemister(106) report the following conditions as being responsible for hypotension; anaphylaxis, histamine administration, spinal cord section, high spinal anesthesia, trauma to the extremities, hemorrhage, plasmopheresis, manipulation of the intestines, and upper abdominal manipulation. These factors have been repeatedly mentioned in the literature and most writers acknowledge their influence as being of etiological significance.

Cobb(33), in the same year, noted than in some persons, by placing pressure on the carotid sinus, the blood pressure would suddenly decrease. This, however, was only a transitory affair and the arterial pressure would assume its normal level as soon as the pressure was released. Brams, Katz and Kohn(24) also in 1933, determined the effect of abdominal distension and release, upon the arterial pressure. They observed that the factors involved in such a fall in the blood pressure may arise either in the venous, capillary, or arterial systems. They thought it con-

ceivable that the intraabdominal veins, compressed during abdominal distention,may act as a reservoir for blood otherwise returning to the heart, when the distention was abruptly released. They, also, concluded that blood from other regions might flow into these comparatively empty veins, thus reducing the return to the heart, causing a consequent fall in the arterial pressure. In doing further work, however, they discovered that a much simpler explanation could be found in the arterial system itself. The rapid release of the abdominal distension quickly reduces the peripheral resistance by abruptly releasing the partially compressed abdominal aorta. This, they found, resulted in a quick and abrupt fall in the arterial pressure before the unequally distributed blood in the venous system returned to a normal balance.

In the same year, Freeman(54) observing the blood pressure of schizophrenics believed that habituation was of etiological import. His subjects were tested each day, under the same conditions, and reports were made every three months for a period of nine months on their blood pressure. He excluded such factors as season, nutrition, anemia, and oxygen consumption as being influential in this series. He, also, assumed that the sedentary life was not an essential finding. On determing the blood pressure, he found that the average reading for the first three months to be 105 m.m.Hg., the second period of three months to be 99.6 m.m.Hg., and the last three month period to be 100.3

m.m.Hg. From this series of schizophrenics, Freeman concluded that the fall in systolic pressure was attributed to habituation of the environmental situation.

In 1934, Hamon and Harkins(65) noted that the blood pressure fell in their experimental animals in which they were producing peritonitis by the injection of bile and bacterial filtrates. They prepared their animals by leaving a loop of the lower ileum, about 40 c.m. in length, attached to its mesentery, and then reestablishing the continuity of the bowel by an end to end anastomosis, the open loop being returned to the abdomen and the wound then closed. They, then, induced peritonitis by the administration of bile and other substances. Washings were, then, taken from the abdominal cavity of the animals and centrifuged. The supernatent fluid was then injected into normal dogs and a drop in blood pressure followed that varied from eighteen to eighty millimeters of mercury, after all except the fluid from the bile peritonitis.

In the same year, Phemister and Livingston(100), working together, found that the blood pressure dropped immediately following an injury to the cervical and high thoracic segments of the spinal cord. This, they determined, was due to paralysis of the sympathetic system and resultant vasomotor dilatation. In watching the blood pressure carefully during surgery, they found, also, that it fell when the abdominal wall was being opened, but that it gradually returned to its preoperative

level, without change in the pulse rate, temperature or respiration. They stated that unless the pressure was noted with especial care the change might go on unnoticed. These observations were based on 4733 consecutive major operations. One hundred seventy-five of these cases were operations on the stomach, and of these, in seventeen the blood pressure fell to 80 m.m.Hg., or less. There was a marked fall in twenty-nine cases of the two hundred and nine that presented biliary disease. In forty-five operations on the small intestine, in only two did the pressure fall to 80 m.m. Hg., and in both of these an ileostomy was done. In determining the causative factor in these abdominal reactions, the pathways by which afferent impulses might pass from the disturbed field are the vagi, sympathetic, and the intercostoabdominal nerves to the peritoneum and abdominal wall. The most plausible theory, according to these authors, seems to be the stimulation of the vagi and carrying of impulses to the medullary center, although this has, as yet, not been proved. The method of action of impulses is still disputed. They may lower the blood pressure by stimulation of vaso dilator centers,or by inhibition of the vasoconstrictor center.This theory is denied by Howell, but upheld by Rosenblewth and Cannon. Phemister stated,"clinically, it is difficult to distinquish between vagus autonomic reflexes and sympathetic or parasympathetic abdominal reflexes because of the overlap of nerve supply and of the diffuse nature of the stimulation in the cases of manipula-

tive and operative procedures and injuries of the abdominal region." They found, in further work, that the blood pressure was reduced following release of a tourniquet placed on an extremity. They were of the opinion that this was due probably to the return of the normal quota of blood to that extremity plus considerable additional blood occasioned by the marked active hyperemia which develops in it. They, also, stated that they thought it possible that the psychic effect precipitated by pain or fear from the injury could have been a factor in causing the hypotension.

Pepper(99), in 1935, stated that although it was a well known fact that exertion, especially if severe and temporary caused hypertension, that if the exertion was prolonged it would effect a lowering of the blood pressure. He, also, stated that in the sclerotic hypertensive, who is bedridden, the pressure may drop and cause a relative hypotension which may or may not produce symptoms. Pepper(97), also, stated that other factors which raised the pressure, such as emotions and fever, if long continued, will cause it to become lower.

Sheard(76), also in 1935, found that following irradiation with a carbon arc a dilatation of the capillaries with an increase in the number of open or functioning capillaries of the skin and superficial tissues occurred, thus producing a diminished peripheral resistance. He, also, noted that irradiation of the skin disturbed the balance between the peripheral sym-

pathetics and the splanchnic parasympathetic tone. Another finding that he reports is the liberation of a substance with histamine-like properties and actions, leading to dilatation and increased permeability of the blood vessels. He concluded, therefore, that following irradiation with a carbon arc one would expect to find a lowering of the arterial blood pressure.

In 1936, Apel(7) did some experimental work with the short wave and its effect on the blood pressure. A spark gap apparatus, Thermidon A, was used with wave lengths of ten to fourteen meters. This apparatus seemed to have more effect on the systolic blood pressure than on the diastolic, and more on older patients than younger. Apel could find no pathological changes in the arteries and concluded that the short waves must exert their effect in some other way, probably through the nervous system. There can be found no positive proof of any chemical change produced by the short wave which in turn would have the effect of reducing the blood pressure. In the same year, Schittenhelm(7) stated that he was of the opinion that certain high frequency currents lowered the blood pressure by affecting, in some way, the sympathetic nervous system. Also, in 1936, Laurens (75) noted that following carbon arc irradiation, the peripheral resistance in the small cutaneous arteries and the middle sized arteries was diminished and that this probably lowered the blood pressure by taking part of the load off of the heart. This same finding was made by Sheard in the previous

year who also thought that the liberation of a histamine-like substance had some effect on the vasomotor tone.

Adair, Hunt and Arnold(1) reporting on the vascular collapse in toxemias were of the opinion that the fall in the arterial pressure was due to first, the toxemia itself, second, the delivery of the baby with its associated hemorrhage and, third, paralysis and massive ectasia of the splanchnic capillary bed.

Wilson and Roome(122) experimenting with animals on which tourniquets were placed, much the same as did Phemister and Livingston two years before, made similar observations, that following the release of the tourniquet there are several factors which one must consider in solving the etiological problem of the hypotension. These men stated that when the tourniquet was released there was a very transient fall in the blood pressure with recovery, followed by a more gradual and more pronounced fall which continues in the experimental animal until death. It is thought that the primary fall is due to the relative hyperemia of the limb(described by Bayliss in 1924), and the absorption of toxic metabolites. The secondary fall is due probably to the formation of toxic tissue metabolites or of the products of anerobic bacteriolysis in the ligated limb, and their absorption on release; also, to withdrawal of fluid from the circulation to be poured out into the limb as a transudate in sufficient quantities to embarrass the general circulation.

ORTHOSTATIC HYPOTENSION

Erlanger and Hooker(46), in 1911, theorized that when the standing position was assumed from the recumbent or the sitting posture, that the blood pressure may either rise or fall, the result probably depending largely upon attendant circumstances such as external temperature, activity of the digestive organs, et cetera. They concluded that the changes in the circulatory conditions, when the erect posture was assumed, were induced mainly by the action of gravity and that they were probably elicted by "bleeding" into the lower extremities. Normally, the effect would be compensated for by a peripheral constriction and by an increase in the energy of the heart. In conditions in which there is a deviation in this normal, however, there will be a subsequent lowering in the systolic blood pressure.

Bradbury and Eggleston(22) were the next to recognize this condition, and in 1926 stated that, "diminution of normal sympathetic tone was suggested by the absence of cardiac acceleration following vagal depression by atropine, and by failure of the heart rate to rise in response to sharp and very great lowering of the blood pressure when the erect position was assumed".

Ashworth(8), in 1929, was of the opinion that orthostatic hypotension was caused by a paralysis of the sympathetic vasoendings. He continued that this would account for the absence of vasoconstriction after the use of epinephrine.

In the following year, Riecker and Upjohn(103), working

together, reported a case of orthostatic hypotension and determined the etiological factors in their case to be an inability of the vasomotor mechanism to respond normally to changes in position, and secondly, cerebral arteriosclerosis with predilection to the vasomotor mechanism. They found the peripheral vasomotor endings to be intact by their response to epinephrine and ephedrine.

Christ(61), in 1931, gave a very clear explanation of the mechanism of the normal response of the blood to various postural changes. He stated that a decrease in the venous return incites the cardiac mechanism to increased rate, in order to maintain equality of cardiac output in the erect posture. Through the agency of vasomotor stimulation, a vasopressor response takes place in the peripheral circulation(splanchnic area especially) to oppose the hydrostatic effect of gravity, and to maintain sufficient diastolic level to preclude anemia of the brain. In cases of orthostatic hypotension, however, there is a defect in the normal vasomotor tonus. There seems to be a paralysis inhibition, or disfunction of the nervous mechanism of vasomotor control, which in turn is influenced by the circulating hormones of glandular secretion. Another explanation may be due to atony or paralysis of the myoneural juncture in the peripheral (especially splanchnic) vessels, or perhaps a change in the character of the walls of the blood vessels themselves.

In 1933, Barker(12) reviewed the literature on orthostatic

hypotension, from the cases reported by Bradbury and Eggleston(22), in 1926 and up until 1933, and found that in the cases thought to be organic,there was little to suggest etiology. He did grant, however, that the case reported by Sanders in 1931, did present an etiological factor-that of trauma due to injury of the abdominal sympathetics. He,also,admitted gonadal insufficiency in view of the loss of libido and potentia. In conclusion, he stated that the disturbance was probably in the sympathetic nervous system, probably peripheral, and probably not disturbing the myoneural structures primarily. Persistance of the condition, however, would seem to indicate an organic basis, he admitted.

Woltman(124), in 1934, was of the opinion that a lesion in the hypothalamus, or a more caudally placed lesion, may upset circulatory homeostasis through interuption of the sympathetic pathways and,thus,cause the blood pressure to fall. He interrogated as to why there were not more cases of hypotension reported in brain tumors or encephalitis and remarked at that time that perhaps it was because they were merely overlooked.

Croll, Duthie and McWilliams(37), in 1935, thought that it may be the posture plus the immobility of the lower limb that caused hypotension, while Code and Dingle(34) stated that they believed the etiological factor concerned was the failure of the carotid sinus to react rapidly to changing intracarotid pressure.

P A T H O L O G Y

Pike and Coombs(101), in 1917, did some experimental work on different staining reactions following cerebral anemia, such as might occur in cases of hypotension. They found that when the cells of the brain and the medulla oblongata were deprived of blood for a period of from ten to twenty minutes, a change in the staining reaction of the cells was demonstrable; if the brain and upper portion of the spinal canal were removed some minutes after the circulation to the head had been restored. They concluded that this reaction would occur in cases of low blood pressure where insufficient blood reached the brain.

In the same year, Bedford(16) noted that increased quantities of epinephrine were thrown into the blood during conditions of low blood pressure and shock. With this increase in the epinephric content of the blood a hyperactivity of the adrenal glands occurred, and in their opinion, this was not due to the substance stored in the gland. They found that the epinephrine increased only after a prolonged continuation of the condition leading to shock, and that it increased in proportion to the length of the period of lowered arterial pressure. They concluded that this increase may have been the last effort of the organism to ward off fatal termination due to the low blood pressure.

Levison(78), in 1924, stated that the blood findings in hypotension were variable and they depended on the various pathological conditions that coexisted with the low blood pressure.

Ferrannini(49), writing in 1931, said, "In 1903, I showed that patients suffering from constitutional angiohypotony have a functional insufficiency of the adrenal capsule and the sympathetic nerve supply, as a symptom of endocrine disturbance".

ORTHOSTATIC HYPOTENSION

Mortensen(89), in 1923, stated that in case the blood pressure dropped more than six to eight percent of its systolic reading, in changing from the reclining to the erect position, it may be viewed as evidence of myocardial insufficiency.

Bradbury and Eggleston(22), three years later, noted that in the three cases that they reported that there was almost a total loss of peripheral vascular tone, and a disturbance in the functional activity of the vegetative nervous system. They, also reported an impairment of the sympathetic accelerator control of the heart and a lack of response of the vagi to changes in position. They, also, noted that there was a paralysis of the sympathetic vasoconstrictor endings, and an absence of response to epinephrine. This paralysis explains the total absence of the normal vasomotor control by which the blood pressure is maintained at a nearly constant level, in the face of changes in the position of the body, in normal persons.

In 1928, Ghrist and Brown(59) reported the work done by Hill and Barnard in 1897 on experimental animals in which they produced low blood pressure. They were of the opinion that in case the vasomotor tone was intact, the splanchnic area formed a resistance box for the circulation, which minimized the effect of gravity. They concluded that in man, a deficient vasomotor tone with an atonic abdominal wall or patulous abdomen, leads to deficient circulation and consequent anemia of the brain.

Barker(12), in 1933, is quoted as saying, "One might consider that the disturbance is due to a partial hypofunction of the myoneural and neurosecretory end-plates, and that only with vigorous stimulation of these, ephedrine or pilocarpine, could the smooth muscle be made to contract and the sweat glands to secrete." He, also, was of the opinion that the condition was manifest; first, by the loss of the reflex(postural or orthostatic) vasoconstriction necessary to maintain normal blood pressure against the force of gravity; second,by hypohidrosis or anhidrosis; and third, in advanced cases, by the loss of reflex acceleration of the cardiac rate. Atropine failure to increase the cardiac rate may be explained by the fact that although the effect on the vagus is inhibited by the drug, the accelerator nerves are not functioning. The accelerator effect of ephedrine and epinephrine are due probably to the direct stimulation of the heart. He, also, observed that the diarrhea and constipation that have been reported may be due to hypofunction of the sympathetic system.

Chew, Allen and Barker(32), in 1936, were also of the opinion that there was a loss of orthostatic vasoconstriction necessary to maintain a normal blood pressure against the force of gravity. They reported, too, that there was a hypofunction of those parts of the sympathetic nervous system which regulate sweating, vasoconstriction, and acceleration of the rate of the heart. They found that the administration of pilocarpine produced sweating, however, and acted on the myoneural junction, therefore, the disturbance would

seem to be central to the action of the drug. Two years previously, Adson and Brown, found that there was a loss of sweating distal to the level of the nipple and a relative fall of the blood pressure when the patient stood erect after an anterior rhizotomy. After resection of splanchnic nerves, the celiac ganglion, and the first and second lumbar ganglia, they noted an anhidrosis distal to the knees and a relative fall in the blood pressure on standing. Quoting Chew, Allen and Barker(32), "It appears, therefore, that surgical removal of peripheral sympathetic nerve fibers produces two changes which are observed in orthostatic hypotension. This observation is evidence that the situation of the fundamental disturbance in orthostatic hypotension is in the peripheral sympathetic nervous system. This belief is further supported by the inconsistency of evidence of involvement of the central nervous system by distribution of anhidrosis in zones which frequently could not apparently result from a central lesion, and by the observation of Sanders that in one patient orthostatic hypotension followed an abdominal injury. These observations, however, do not preclude the possibility of disease of the central part of the sympathetic nervous system and no definite conclusions can be drawn. Whether the deficiency in sympathetic nervous system is organic or functional is entirely unknown."

I N C I D E N C E

According to Potter(102), Reitter was the first to report true hypotension to be associated with tuberculosis. In 1907, he found that lowered blood pressure existed in cases of tuberculous nephritis, whereas, in other forms of pyelitis and pyelonephritis the blood pressure was characteristically increased or normal.

Edgecombe(43), in 1911, stated that he had patients who did not present any definite disease entity but who complained of general weakness, lackness, and want of tone. In doing a physical examination on these persons, he found that the systolic blood pressure was consistently low, usually below one hundred millimeters of mercury. In the same year, Emerson(102) observed two hundred cases of pulmonary tuberculosis, found hypotension to be universal, and believed it to be on a basis of emaciation. Bailey,(1) also in 1911, reported six cases of shock following delivery of patients with eclampsia and preeclampsia, all with extremely low systolic blood pressure.

In 1912, Faught(48) found that low blood pressure was present occasionally in the terminal stages of aortic regurgitation, or when cardiovalvular disease was accompanied by myocardial, arterial or renal degeneration. He noted, also, that it may accompany extreme narrowing in mitral stenosis. In a few instances, he observed a lowered pressure with alterations in the heart rate, more especially with bradycardia and parox-

ysmal tachycardia. Faught(48) was also of the opinion, as was Reitter, that low or lowered arterial pressure was practically the rule in tuberculosis. Many authors believe that, if consistent, it indicates infection with the tubercle bacillus even without other clinical manifestations. Reitter(102)suggested that hypotension associated with nephritis was always tuberculous. Further, Faught(48) indicated in his work that in general paresis low blood pressure was a constant finding unless there was present some renal disturbance, as well.

It has been said that typhoid fever is more frequently accompanied by hypotension than any other acute infection. Cases of typhoid usually present a systolic reading of between ninty and one hundred millimeters of mercury. Barach(48) is of the opinion that the pressure falls from normal when the patient goes to bed and remains down until convalescence is established. He adds,further, that a steady fall in the blood pressure indicates a poor prognosis.

Hypotension is so common a finding in pneumonia, especially the lobar type,that Gibson made the following rule. "When arterial pressure expressed in millimeters of mercury does not fall below the pulse rate expressed in beats per minute the fact may be taken as of excellent augury, while the converse is equally true." This rule is still followed to some extent and points out how universally hypotension accompanies pneumonia.

It may, also, be said that hypotension is the rule in

cholera, and present usually in diphtheria, scarletina, rubella, and acute rheumatism. It is, also, associated quite commonly with wasting diseases such as carcinoma and other cachectic states. Diabetic and epileptic coma are other conditions in which hypotension is found. It is so universal in epileptic coma that it may be used as a diagnostic point between that and uremic coma.

Potter(102), in 1915, observed that persons with orthostatic albuminuria frequently presented symptoms of diminished pressure. He also noted, as did Barach, that typhoid fever is nearly always a hypotensive disease.

In 1919, Dearborn(40), stated that he thought that there were a number of over-studious or over-worked young persons of each sex, but more females, whose systolic pressure was in the ninties for short periods of time. He noted that these persons did not have perceptible myocardial weakness or valvular leaks and were capable of a great deal of work-some of them being college athletes.

In the following year, McCrae(79) classified one hundred cases of low blood pressure as follows:

1. Nervous disturbances----------38 cases
2. Myocarditis----------25 cases
3. Internal secretion disturbances------- 8 cases
   a. Hyperthyroid----------3 cases
   b. Myxedema---------- 2 cases
   c. Polyglandular disturbances 3 cases
4. Anemia---------- 3 cases
5. Miscellaneous----------26 cases
   a. Nephritis

b.Syphilis
c.Arthritis
d.Epilepsy

Hoxie(70) stated, in 1921, "The frequency with which low blood pressure is associated with vesiculoprostatitis in the male, and with some disturbance of the ovarian function in the female, has tempted me to dogmatize and say that low blood pressure is practically always accompanied by some lesion in the genital tract". In this same year, Hoxie(70) also reported that he was of the opinion that women in the child bearing age had lower blood pressure readings than at any other time of life.

Swartz(1), in 1923, reports findings similar to those observed by Bailey about ten years previously. Among sixty eight patients with toxemia thirteen of them developed post-delivery shock, accompanied by low arterial pressure readings. This series of cases showed an incidence of nineteen percent.

In the following year, Friedlander(55) made observations similar to those of Faught, but went a little further and attempted to explain his findings. He was of the opinion that in cholera, the decreased pressure might be due to the loss of plasma from the circulating blood. In diphtheria, he explained that the myocardial degeneration with the corresponding lessened cardiac output, along with the action of the toxins on the respiratory center were probably the causes of the hypotension, although Stejskall, in 1914, was of the opinion that the toxins acted directly on the heart. In malaria, he is of the opinion that the

plasmodium plug the capillaries and thus cause the change in the pressure. And lastly, he thinks that myocardial insufficiency and vaso dilatation resulting from the toxins on the vasomotor center seem to be the etiological factors concerned in causing hypotension in tuberculosis.

Levison(78), in 1924, was the first to report that certain constitutional types showed special predilection toward hypotension. He stated that those individuals presenting a slender build, narrow slender thorax, small bones, long abdomen, long and narrow heart, dyspnea on exertion, palpitation, precordial pain, headaches, and cold extremities were apt to have a low systolic pressure.

In the next year, Barach(10) collected the following data as to the incidence of hypotension: One; at a marathon race in 1910 there ware entered fifty five runners. Three of these men had low blood pressure and of these three, one dropped out in the first three miles, another ran ten miles and was forced to stop, and the third ran thirteen miles before having to drop out of the race. All of the other runners were able to finish the race, indicating their higher reserve power.

Two; At the Carnegie Institute of Technology in 1914, 656 students were given a physical examination. Twenty-three of these had a systolic pressure of between 100 and 110 m.m. Hg., and seven between 90 and 100 m.m. Hg., or an incidence of four percent.

Three; During the war, several experiments were carried out,

one of these at Camp Sherman in 1918. Of 31,596 recruits examined here,1315 were referred to a cardiovascular board for further examining. Of these,73 had a systolic pressure below 110 m.m.Hg. and thirteen of these were rejected because of definite cardiac disease. --an incidence of five and one-half percent.

Four; At another examination at Camp Sherman, 27,224 recruits were processed and of these, 1016 were sent to the cardiac board for further check-up. This time twenty-four were rejected because of hypotension, an incidence of two and three tenths percent.

Five; Alvarez, in 1923, reported an incidence of two and two-tenths percent in 6,000 students at a California university.

Six; At the Carnegie Institute again in 1924, 1100 male students were examined and fifteen had blood pressure readings of 110 m.m. Hg. and nine of the men had readings below this, an incidence of 2.5 percent.

Seven; In his own series of forty-six patients past middle life, ages 40 to 80, five had a systolic pressure below 110 m.m Hg. The incidence in this series was approximately 11 percent. In recording his cases of typhoid fever and influenza, he reports that in eighty-one cases of typhoid the average systolic pressure in the first week of the disease process was 93 m.m. Hg., the second week, it was 92, the third and fourth weeks 83, fifth week 85, and the sixth week back up to 90 m.m. Hg. The fifty cases of influenza that he saw had an average blood pressure of 89 m.m. Hg.

In the next year, Stengel(112) found that anoxemia was fre-

quently attended by low blood pressure. He, also, was of the opinion that it tended to be lower in children than in adults, and that it accompanied infections, gastrointestinal distress and toxemia, anemias and cardiac weakness. He noted that the individuals were frail, slender, narrow chested, and ptotic types.

In the same year, Fossier(52), stated that eight to ten per cent of all females had a lowered systolic blood pressure. He, also, reported Alvarez's and Barach's finding that a series of 10,142 males had an incidence of hypotension of 3.55 percent.

Cheney(31), also in 1926, reported a case of trichinosis associated with low blood pressure which fell to 44/18 on the second hospital day. He injected 1 c.c. epinephrine subcutaneously and the pressure immediately rose to 118/48 and did not fall again. This type of hypotension has been reported by Gruber and other German writers, but is not generally noted in this country.(Von Gruber, G.B.Muchen med. Wchnschr. 72:1193, 1925)

In 1927, Tung(115) reviewed the Chinese literature and noted the the blood pressure in the Chinese race was lower than that in the white races. The following chart is borrowed from him showing the data that he collected, and the original articles that he reviewed.

AUTHOR	PATIENTS	AGE	BLOOD PRESSURE
Kas(Nat. M.J. China 8:101, 1922) Hunan(Central China)	63	21-25	116
Kas(Nat. M.J. China 8:101, 1922) Hunan(Central China)	10	26-42	113
Cadbury(China M.J. 37:823, 1923) Canon(South China)	700	15-30	101

Kilhorn(China M.J. 40: 1, 1926) Szechuan(West China)	741	14-31	111
Ying(China M.J. 40:641, 1926) Shaoshing(East China)	182	21-50	113

Williams(120), in 1929, in discussing low blood pressure associated with pregnancy, said that five percent of the women having low blood pressure mature late and are relatively infertile. He observed fifty cases, most of them being in the third decade of life; thirty two of them were primiparous, and were married three to ten years before their first pregnancy. Nineteen of these women had used no contraceptive and five of them had operations to remove the cause of their sterility. The eighteen multiparous women had twenty-one children and six abortions.

In 1930, Vaughan and Graham(116) reviewed the literature of hypotension in the south and reported at the same time their original work. They found in their own series of 4000 cases(office patients) an incidence of hypotension of five and one-half percent. Roberts in Atlanta reported an incidence of eighteen percent in 1,950 of his private patients, and Henry in Memphis stated that in 300 clinic cases he found an incidence of 12.4 percent. Limbaugh reported the highest incidence of all, in examining fifty four applicants for life insurance, he found that forty-four percent had low arterial tension. Colonel Brooks and Colonel Siler of the United States Army, also, noted that the average systolic pressure in the Phillippines was lower than in the United States and Aries of Panama City made a similar observation.

In 1931, Brockington(25) stated that in all cases of faucial diphtheria, there is a drop in the blood pressure usually beginning on the seventh or eighth day.

Freeman(53), in 1932, in determing the average blood pressure of schizophrenics observed it to be 11.2 m.m. Hg. lower than that of the normal individual of a corresponding age. This test was carried out on a series of 180 patients of an institution.

In the same year, Meakin(85) reported six cases of hemolytic jaundice with the hemoglobin above ninty and the blood pressure average of 95 m.m. Hg., as compared to a normal of 120 m.m Hg. He, also, presented a chart of one hundred consecutive cases of catarrhal jaundice showing the blood pressure to be below the level for that particular age group. A reprint of the chart is given below; and up until the sixth decade the pressure is shown to be universally lower than normal.

DECADE	CASES	SYSTOLIC PRESSURE	NORMAL SYSLIC PRESSURE*
2	14	104	115
3	36	113	121
4	16	114	123
5	12	109	172**
6	14	134	131
7	4	148	?
8	4	155	?

Note: * Determined from 545,121 patients
** Perhaps a misprint

Hoyle(71), in 1934, was of the opinion that acute hypotension was found in acute illnesses, hemorrhage, surgical shock, severe fevers, coronary thrombosis, and in cases where there was rapid effusion into the pericardial sac. Separate from the acute

forms, he goes further, and states that the chronic type of hypotension is found in wasting diseases and in mitral and aortic stenosis.

Adair, Hunt and Arnold(1) report that there were twenty six cases of toxemias of pregnancy in which the blood pressure dropped more than seventy millimeters of mercury. This data was collected from the Department of Gynecology and Obstetrics of the University of Chicago Lying In Hospital, from the year 1931 to 1935.

Chew, Allen and Barker(32), in 1936, reviewed the literature of orthostatic hypotension and found twenty-six reported cases in the United States, two in England and three in France.

S Y M P T O M A T O L O G Y

In the series of case histories that have been observed the hypotensive individuals present many symptoms in common. They practically all complain of weakness and vertigo. Goodman and Williams(102), in 1914, presented cases in which the patients were weak, had constant backache, suffered from dizzy spells, and were unable to concentrate as they could previously. Six years later, McCrae(79) noted the same findings in patients of his, and also observed that they were very easily fatigued, upon the slightest exertion. Graham-Stewart(63) in 1928 went further and stated that the hypotensive was apt to show cyanosis of the extremities, a livid skin, and sensitivity to the cold. He, also, was of the opinion that constipation was the rule in persons presenting these symptoms. In the same year, Upjohn and Reicker(103) presented a patient with hypotension who had complained of convulsive jerkings of the arms, and who had also been suffering from a blurring of the vision. Quoting Pepper(98), in 1935," the patients are below par and are easily fatigued".

The patients with orthostatic hypotension, however, present much the same symptoms only they have their complaints when they are in the erect posture, being relatively symptomless in the recumbent position. The patients will usually complain that they have not been able to sweat since they first noted their weakness, and this deficient sweating may be generallized or merely localized. Chew, Allen and Barker(32), in 1936, noted an accentuation

of the symptoms in hot weather, and an excretion of a larger amount of urine when the patient was recumbent than when he was erect. Appearance of youthfulness not in accordance with the actual age is another relevant sign that the orthostatic hypotensive will frequently present. In other cases, it has been noted that the basal metabolic rate is somewhat lowered. Loss of sexual desire, which is sometimes associated with impotency is another finding that is present in some individuals with orthostatic hypotension. Finally, they may have a marked pallor of the skin which they had not noted themselves.

Patients with a lowered systolic blood pressure usually have very vague symptoms which do not seem to point to any distinct disease entity. They complain of lassitude, lack of energy, easy fatigability, lack of interest in their surroundings and occupations; they are frequently depressed, and some of them also complain of gastrointestinal symptoms. On the other hand, the person with a lowered pressure may be full of ambition and have no symptoms which would lead him to the physician. As has been pointed out previously, there have been college athletes that have come for a physical examination, and not until this time have they known that they fell in the category with certain other individuals who were constantly depressed and suffering from inumerable symptoms.

D I A G N O S I S

The diagnosis of hypotension is established definitely by the use of the sphygmomanometer. It is the duty of the practicing physician to take the blood pressure of each and every one of his patients, and most especially of those who have presented symptoms that would tend to indicate an alteration in their arterial tension. The symptoms that individuals present in hypotension have been discussed in the chapter on symptomatology and will not be reiterated here.

The diagnostic powers of the clinican will be taxed somewhat more in the patient with orthostatic hypotension, as the symptoms in this condition appear only after the patient has arisen from the recumbent position, and in some cases this fact is difficult to elicit from his story of his present illness. It has been fairly well established, however, that the orthostatic hypotensive presents a rather clear cut diagnostic entity, and the physician, with the aid of his sphygmomanometer, should have little difficulty with differential diagnosis.

P R O G N O S I S

The prognosis, as concerning life of the individual with hypotension, may be said to be relatively good assuming, of course, that the arterial pressure does not encroach upon the level of shock. It has been definitely established that the person with hypertension will probably not live to his normal expectancy, while quite the reverse is true of the hypotensive. Bishop(97) has advisedly written, "—the patient with hypotension lives to a miserable old age".

As concerning morbidity, the prognosis seems to be variable. Some persons may have a systolic pressure that is below the accepted normal and yet suffer no untoward symptoms, whatsoever, while others will be attended by weakness, vertigo, and the other cardinal symptoms of low blood pressure, unless they treat their condition daily.

A patient should be promised nothing as to prognosis until his case is thoroughly understood, and only then reservedly.

Muhlberg(57) is quoted as saying, "—there appears to be no doubt of the fact that low blood pressure, past the age of fifty, unassociated with any organic lesion to account for this low blood pressure, is the best criterion that we possess that the individual will live beyond his normal expectancy".

S E Q U L A E

Hypotension in Tuberculosis

The incidence of tuberculosis in hypotension has been discussed previously, however, nothing was said regarding the mechanism producing the fall in pressure. It has been suggested by Emerson (45), in 1911, that the toxic action of the tubercle bacillus products may exert some effect on the myocardium causing a weakness of the cardiac tissue, thus reducing the output of the heart.

Another theory that has been advanced is that of the diminished area of lung tissue, resulting in an increased carbon dioxide content of the blood. This theory seems to be contradicted, however, and is probably not the true mechanism at all.

The essential fact to be remembered, however, is that in nearly all cases of pulmonary tuberculosis, one will find the condition of hypotension associated with the pulmonary involvement.

Hypotension in Schizophrenia

It has been reported, previously, that in a series of schizophrenia, 180 patients examined by Freeman(53) that the blood pressure was 11.2 m.m. of Hg. below that of the normal for their respective ages.

Freeman made several other observations in this group which will be enumerated here.

1. The blood pressure did not vary with age until the fifth decade.
2. There was no constant variation of the pressure with different seasons of the year.
3. Duration of hospitalization seemed to have no effect on the arterial tension, and the nutrition factor was insignificant.
4. The psychotic groups varied but little in their mean systolic pressures; the paranoid groups had the highest and the catatonic, the lowest readings.

From these observations, it may be concluded that low blood pressure universally accompanies schizophrenia.

Diphtheritic Hypopiesia

As has been stated, previously, hypotension frequently accompanies diphtheria. In many cases, the pressure drops only a few millimeters, while in the more severe types of faucial diphtheria, it may drop markedly.

Brockington(25) has stated that after a latent period in the disease process, there is a progressive fall, followed by a rise in the blood pressure. The pressure does not fall below the normal until about the seventh or eighth day of the disease--and reaches its lowest point sometime before the twelfth day. It has been said, with a fair degree of accuracy, that the depth of the blood pressure curve is in direct relationship to the severity of the disease.

In summarizing, it may be said that this condition of diphtheritic hypopiesia, which occurs late in the process of the disease, accounts for about fifty percent of the deaths during the first three weeks, and is clearly distinquishable from the early classical cardiac failure.

Hypotension in Surgery

McQuiston(80), in 1934, determined the relationship of arterial hypotension to surgical risk. He reported on a series of 250 patients and made the following observations:

1. The blood pressure of all patients was 100 or less millimeters of mercury. 36 had pressure of 90 m.m. or less.
2. Types of surgery done.
   a. Cholecystectomy-63 females, 37 males.
   b. Gall bladder or stomach-11 females, 89 males.
   c. Major pelvic-50 females.
3. Age of patients.
   a. Second decade - 2
   b. Third decade -35
   c. Fourth decade- 77
   d. Fifth decade -77
   e. Sixth decade -41
   f. Seventh decade-17
   g. Eighth decade - 1
4. Deaths attributed to the surgery done occurred at ages of 56, 60, 64, 75, showing that elderly persons with hypotension are the greatest surgical risks.

T R E A T M E N T

Since the days of the middle ages the profession has administered whole blood to persons suffering from the results of hemorrhage(Clendening) and following this they began the use of other liquids to build up the lowered blood volume. It was not until 1896, however, that Starling(14) emphasized the importance of the osmotic pressure of the protein content of the blood and the tissue fluids in the passage of water from one to the other. In that year, he stated that the protein content of the blood plasma was higher than that of the tissue lymph, so that there is a continual attraction of water from the tissues to the blood. This is, however, normally balanced by filtration in the other direction, which occurs when the pressure in the blood vessels exceeds the difference between the osmotic pressure of their contents and that of the tissue fluids. The colloid added to increase the viscosity of an intravenous injection must, therefore, possess an osmotic pressure equal to that of the colloids of the blood. It is desirable, therefore, in the opinion of Starling, to increase both the viscosity and the colloidal osmotic pressure of the intravenous solution used in regaining the blood loss.

Edgecombe(43,48), in 1911, treated collapse in cholera with 500 c.c. of a solution of adrenalin 1:250,000, injected intravenously. He found that circulatory response was immediate and that the pressure rose to almost its normal height. In the following year, he treated a case of low blood pressure in which he

thought that the cause due to poor circulation, with hot baths, exercise and massage. He stated that he was of the opinion that hypotension,due to an infectious process, should be treated symptomatically, and that the hypotension would clear up of its own accord.

Goodman(62),in 1914, treated several cases of low blood pressure by prescribing regular exercises in the morning, mild outdoor exercise during the day and nux vomica, gtts. xv t.i.d. He, also, advised the patients to give up alcohol, tobacco, coffee, tea, et cetera. He stated, "I am inclined to believe that of all of the measures to employ in raising blood pressure in such cases, the least to be considered are drugs."

In the following year, Potter(102) used dried adrenal substance in seven of his cases which presented a lowered systolic pressure. He used the substance in doses of from two to four grains, three times a day, and found that five of the cases improved, one failed to improve and one died. In using nicotine to increase the respirations, Simond(110),in 1916, discovered that beneficial results were obtained in circulatory shock, but not in hemorrhage. He was of the opinion that low blood pressure due to anaphylactic shock and peptone poisoning did not respond well to epinephrine but did to nicotine. He theorized that it may be due to the condition of reduced irritability in the vasomotor center, and since the results of nicotine are mechanical, that the effect was due to the increase in respirations. The dy-

spnea so produced causes a suction on the overfilled non-collapsible veins of the liver and brings sufficient blood to the underfilled right side of the heart and ultimately to the systemic vessels.

Lawrence(77), in the same year, stated that, "the condition demands further study". He maintained further that sedatives were usually harmful, but that atropine in small doses seemed to aid the condition materially.

Downs(14), doing experimental work on laboratory animals, found that if the blood pressure had fallen to three-eighths its normal level, that intravenous injections of saline could only restore it to two-thirds normal. He, also, stated that if part of the blood was replaced by saline the viscosity of the blood would be decreased and thus have a decreasing effect on the pressure. Bayliss(14), in 1916, found that gum or gelatine solutions, although more effective than pure saline, produced a much less permanent rise in cases of vasodilatation than in cases of blood loss. The combination of a small dose of barium chloride(Langley) with a moderate amount of gum solution was found to be the most satisfactory method of treatment in cases of vasodilatation, and no diminution of vasomotor excitability resulted.

Pike and Coombs(101) were the first to report in the literature the use of oxygenated blood in the treatment of cases of low blood pressure. Simond(111) also noted that by using carbon dioxide in low blood pressure, that the dyspnea so produced elevated the arterial tension. He, also, observed that the pressure reached normal le-

vels sooner in cases of peptone poisoning than it did following the injection of fat emboli.

In the same year, Bayliss(15) advised the use of a six to seven percent gum solution to replace the blood loss caused by hemorrhage producing a lowering of the blood pressure. He was of the opinion that even a two or three percent solution would be better than the use of saline solutions to increase the pressure.

In the following year, Auer and Meltzer(9), did some experimental work with the injection of epinephrine. They discovered that the effect of the drug would pass off in about ten minutes after the intravenous injection. They, also, observed that following injection of the drug into the spinal canal that the effect lasted over thirty minutes and that the blood pressure would rise even above its original level. They concluded from these experiments that the initial dose in treatment of low blood pressure should be about 3 c.c. of a 1:1000 solution of epinephrine.

McCrae(79), in 1920, said that the most important treatment in low blood pressure was prophylaxis--to find the etiological factor and treat that. He suggested oral epinephrine 1:1000 gtts. xv t.i.d. in cases of glandular disfunction. He concluded that if the hypotension was on a menopausal basis the best treatment was the use of corpus luteum, or some like substance. However, if the symptom was merely of a nervous type he recommended adequate rest and moderate exercise, preferably outdoor.

Hoxie(69), in the following year, was the first investigator to try endocrine therapy in the treatment of low blood pressure. He even ventured the opinion that adrenalin and substances from the entire adrenal gland were given to no avail in Addison's disease, and in conditions in which the blood pressure was lowered because of acute infections and exhaustion. He observed that subcutaneous injections of pituitary extract raised the blood pressure twenty to thirty millimeters of mercury in some cases, especially in the nervous individual, and that the effect lasted from twenty-four to forty-eight hours. He also stated, however, that the continued use of this extract did not seem to stabalize the vasomotor system. In using thyroid extract, Hoxie thought that in some individuals it was of definite benefit, but explained that he did not know the rational of its effect. By use of the secretions of the sex glands, especially the extract of the glands of Leydig, and the so-called "ovarian residue", he obtained some very good results. From their action, he thought that there was more parallelism between them and vasomotor tone than there was of the other organs. "The prime requisite, however, is rest, both of mind and body, as vasomotor tone depends on psychic as well as somatic influence".

In 1924, Levison(78) discussed the significance of arterial hypotension and suggested the use of strychnine, hydrotherapy, and digitalis as modes of treatment. He, also, was of the opinion that tight abdominal binders might offer some relief in the enterop-

totic individual. In his discussion he quoted Pal as saying that pituitary extract combined with adrenalin had a more prominent effect than when the latter was given alone.

Miller(87), in 1926, was of the opinion that all forms of treatment for vascular hypotension were unsatisfactory. He did, however, classify treatment into three main groups. First, the acute surgical hypotension of hemorrhage and shock, for which he recommended blood transfusions or the injection of colloidal substances into the vein. The second group in his classification was the symptomatic hypotension of long duration. He indicated that the first type of treatment for this group was treatment of the disease entity itself. He, also, found that in many of these the hypotension was a compensatory affair on the part of nature to lessen the metabolism and strain on the body and, therefore, one should use his clinical judgment as to whether the pressure should be raised or not. Miller(87) did, however, use ephedrine successfully in cases of pneumonia, gastric neuroses, duodenal ulcers, arthritis and acute rheumatic fever, neurasthenia, cerebral thrombosis, and myocardial and valvular heart disease. He claims no clinical benefit, but merely states the fact that ephedrine will raise the pressure in those instances. In the third group, he noted that the patients were asthenic and as a rule had a poor respiratory apparatus, and he thought that the condition may have been congenital. Even a slight increase in the blood pressure in these cases offered improvement in the general health

and mental condition of the patients, and ephedrine proved to be adequate therapy. He started the use of ephedrine after reading of the work of Chen(1925), who injected dogs with histamine and then raised their systolic pressure by the use of ephedrine salts. He noted that the pressure rose to nearly its normal level with adequate doses of ephedrine; one to three milligrams per kilogram of body weight. He explained this action by the increased heat production which tends to increase the circulation through the stagnated areas in the body. Thus, by improving the circulation, the nutrition to the medulla and the vital centers is improved and the body can more easily throw off the toxic effects of the histamine. He asserted, however, that the prompt administration of the ephedrine was essential.

In 1929, Wolfson and Teller(123) experimented with the administration of intravenous gelatine solutions, and found that a five percent solution injected into test animals with lowered blood pressure following hemorrhage, would restore the pressure for several hours. This seemed to produce no untoward effects on the animals. They noted, further, that solutions of saline, dextrin, and starch would elevate the pressure but that they would not maintain it for a very long period of time.

Mortensen(90), two years later, mentioned several ways in which a low blood pressure could be increased. Several of these methods have been mentioned or suggested before, but for the sake of completeness they will be reiterated at this time. For the

more severe types, he recommends 50 c.c. of a fifty percent glucose solution, or 300 to 500 c.c. of blood to be given as a transfusion. For milder cases, and cases in which there has not been a marked blood loss he suggests; first, to remove all possible foci of infection which may be the etiological factor behind the hypotension; second, rest, either moderate or absolute depending on the severity of the case; third, a change in the climate if at all feasible; and lastly, hydrotherapy, massage and heliotherapy.

Burch and Harrison(27), in the same year, noted that the blood pressure always dropped following the administration of a spinal anesthesia. They found that by the injection of a physiological solution of sodium chloride, intravenously, immediately prior to the induction of the spinal anesthesia that the blood pressure did not drop as regularly as it did without the injection. They, also, observed that it was necessary to inject an adequate amount for the effect to be noticeable, and that this amount was about one liter for a normal sized man.

Blalock(20), also in 1931, observed that tannic acid and ephedrine, applied to the surface of burned areas on dogs, were beneficial in raising the blood pressure which so regularly drops following extensive burns. They theorized, however, that the effect so produced may have been due to the prevention of the loss of fluids, rather than any specific action on the vasomotor tone of the animal.

Ferrannini(49), in discussing constitutional angihypotony,

stated that he was of the opinion that dietetic, balneological, climatic and endocrine treatment to tone up and detoxicate the walls of the vessels and the whole organism seemed to be of some value therapeutically.

Two years later, Weiss and Ellis(119) tried several methods to elevate the blood pressure in hypotension. The finally arrived at the conclusion that, "Any vasodilating durg which fulfills the criteria demanded in the treatment of arterial hypotension should have a constant, sustained action, should act by dilating the arterioles over all the constricted areas, should not give rise to unpleasant symptoms or side effects and should maintain the normal function of the organs, particularly of the heart and kidney".

Hoyle(71), in 1934, found that the use of suprarenal cortex, such as eucortone or eschalin, had more effect on the general health of the individual than it did on the creased blood pressure.

Hypertonic, intravenous glucose was given to cats, whose blood pressure had been lowered artificially by experimental trauma, and this solution was found to produce a sustained rise in the pressure. Mazzola and Torrey(83) did this work using fifty percent glucose solution. They found that they obtained the best results by using 2 c.c. per kilogram of body weight. Besides raising the blood pressure, they also observed that the pulse pressure increased while the cardiac rate was decreased. They noted, too,

that a preoperative injection diminished the fall in pressure due to trauma.

Adair, Hunt and Arnold(1) recommended two types of treatment for vascular collapse in the toxemias of pregnancy. They classified these two types as prophylactic and active. The active treatment consists of three parts; first, 20-30% hypertonic dextrose intravenously; second, 30 grams acacia with 4.5 grams of sodium chloride in 100 c.c. ampules, diluted to 500 c.c. of freshly diluted water; and thirdly, the search for some hemorrhagic vessel. The administration of the dextrose should be started immediately and if the collapse is profound, from two to three minims (0.12-0.18c.c.) of 1:1000 epinephrine should be injected by hypodermic syringe.

Walker(117), in 1936, treated fifty-one cases of low blood pressure with hypertonic sodium chloride solution. In forty-nine of these cases, the salt was injected intravenously with the object of raising the pressure before, during or following a surgical procedure: most of the cases treated received 40c.c. of a 30% salt solution and responded in a very few minutes. In the other two cases, a small amount of strongly hypertonic salt was used for its rapid stimulating effect on the circulation. In the first of these cases, the salt was given following an exploratory operation for a cerebral tumor, in order to reduce the intracranial tension which made it difficult to close the dura. Within five minutes the pressure rose from 130 to 165 m.m. of Hg. In

the other of these cases, one of paralytic ileus, there was a marked initial shock with a drop from 120 to 70 m.m. of Hg. 40 c.c. of 30% saline was administered and in five minutes the pressure was again 120 m.m. Hg.

In concluding,it may be said that there are four factors concerned in raising the pressure and that they are:

1. Increasing the force of the hearts contraction.
2. Increasing peripheral resistance by vasoconstriction.
3. Increasing the depth of respiration.
4. Increasing the volume of the circulating blood.

Any cardiac stimulant will aid in satisfying factor one, above. To increase the peripheral vasoconstriction, one may use ephedrine or coramine. Intramuscular coramine injections of about three to five cubic centimeters are beneficial in states of severe collapse. In satisfying factor three, by increasing the depth of respirations, one establishes a greater volume of inspired air and a greater output. This effort improves the oxygenation of all of the body tissues. If one wishes to increase the blood volume, he may use blood transfusions or isotonic salt with gum acacia. For a more rapid response, however, an injection of 40 c.c. of 30% saline solution, intravenously, will raise the pressure rapidly—much more rapidly than the known circulatory stimulants.

So much has been said in the treatment of hypotension about the use of hypertonic intravenous saline that I think that it might be adviseable at this point to review a little of the physiology concerned. When hypertonic sodium chloride solution is injected into a vein, it exerts a high osmotic pressure. Water is drawn

from the tissues into the circulation during the period when the plasma is hypertonic(Peters and VanSlyke) and there is a transitory increase in the plasma volume and a dilution of the plasma protein. The colloidal osmotic pressure is reduced, diuresis results, and the blood volume may then fall below normal by the water lost in the urine. The diuresis,itself,may be of use in helping the body to get rid of acid products and toxic substances produced while there is a diminished activity of all tissues, during the period of shock when there is a reduced oxygen supply and a consequent accumulation of waste material. Following the increase of the sodium chloride in the plasma, there is found a change of color in the individual. Varying the carbon dioxide tension in the blood,alters the distribution of the chloride ion as well as the HCO3 between the cells and the plasma. If the carbon dioxide tension is raised, more HCO3 is formed, combining with part of the base previously bound by hemoglobin forming potassium bicarbonate in place of potassium hemoglobinate. The electrolytic action of sodium chloride may cause a reversal of the reduced hemoglobin to normal oxyhemoglobin. Clinically, the rapid change from pallor and cyanosis to a pink color is seen immediately in the face and hands when extra sodium chloride has been given. The explanation may not be entirely chemical, but in part due to the raise in blood pressure causing better oxygenation of the blood in the lungs.

TREATMENT OF ORTHOSTATIC HYPOTENSION

Bradbury and Eggleston(26) reported in 1926 that the treatment of orthostatic hypotension was unsatisfactory and that efforts to the patients were to no avail. They used thyroxin, epinephrine, dried suprarenal substance, mixed glands, strychnine and digitalis and came to the conclusion that none of these were indicated. They did have some temporary success with ephedrine, however, but did not treat enough patients to determine its value.

Christ and Brown(59), in 1928, also tried ephedrine in the form of ephedrine sulphate and noted some degree of benefit to their patient. They used 25 milligrams five times a day and found that the patient improved so that she could walk and climb stairs, with some difficulty, and only seemed to have distress on very hot days. In reporting to her physicians five years after she started treatment, she said that she was using the ephedrine only twice a day, but was taking it in 50 milligram doses, and could do her work normally.

Christ(61), three years later, stated that he was of the opinion that neither lumbar or cervicothoracic sympathetic ganglionectomy and trunk resection seemed to alter the manifestations of vasomotor tone. He based his opinion on the fact that he had seen patients return with symptoms following this type of an operation.

Allen and Magee(4), in 1934, tried two different forms of

treatment, the use of ergotamine tartrate and ephedrine sulphate. By using 0.5 milligrams of the former, they noted that the pressure was increased and that the symptoms disappeared for a period of one and one-half to two hours. They used the ephedrine sulphate on two patients, using different dosages, and noting the difference in effect. On the first patient, they administered the drug in doses of 25 milligrams every hour from seven o'clock in the morning until eight o'clock at night. During the day, the blood pressure averaged as follows: recumbent 170/120, sitting 130/95, and standing 75/50. At the end of the day, the patient complained of severe nervousness. On the second patient, they used 100 milligrams at six A.M., and 50 milligrams at ten, one, four and seven P.M. The only complaint,after this treatment, was insomnia which was alleviated by the use of pentobarbital or amytal. From these cases, they concluded that an individual regime must be worked out for each individual patient, and they did seem to think that ephedrine sulphate was the drug of choice.

In the following year, Weis(118) stated that by the use of ephedrine sulphate the word "cured" could be used advisedly in some instances.

In 1936, Chew, Allen and Barker(32) came to the conclusion that the treatment of orthostatic hypotension depended on the following:

1. Symptomatic relief, by maintaining the blood pressure to a level where the patient has no distress.
2. Pilocarpine hydrochloride, oral administration of one-

fifth of a grain three times a day for the induction of sweating.

3. Ephedrine sulphate in adequate doses, depending entirely upon the patient, but usually doses of 50 milligrams every two hours.

They, also, were of the opinion that the use of ephedrine was not satisfactory, but that at the present time it is the best known therapy. In concluding, they stated that each individual patient must be worked up carefully and therapy properly instituted as the treatment for one patient will vary markedly from that of another with similar symptoms.

C O N C L U S I O N S

1. When the systolic blood pressure reaches 110 millimeters of mercury, the condition may be spoken of as hypotension.
2. The incidence of hypotension may be said to average about 5% in males, and 8% in females, while only twenty-six cases of orthostatic hypotension have been reported to date.
3. The etiology is not definitely known but the preponderance of opinion points toward some disfunction in the peripheral sympathetic nervous system.
4. Diagnosis of hypotension is made by careful analysis of the patient's past and present illness and by the physical observation obtained with the syphygmomanometer.
5. The prognosis, both as to morbidity and life, is good.
6. Treatment established thus far has been most satisfactory with ephedrine sulphate.

In concluding, it seems as though the profession is slowly beginning to recognize the condition of hypotension and to give it more of their consideration than they have in the past. It is quite true that patients with this symptom do not have the sequlae that are associated with hypertension.

Quoting Hay(66), in 1936, "—It is important to recognize, however, that a low blood pressure is not necessarily pathological: there are many men and women in perfect health, including many athletes, whose cardiac reserve and staying power are ample and in whom the condition is physiological."

Nevertheless, lowered arterial pressure may cause various symptoms in an individual which will entitle him to therapy that the medical profession can offer, and in these cases, treatment should be instituted.

B I B L I O G R A P H Y

1. Adair, F. L., Hunt, A. B., and Arnold, R. E., Vascular collapse in toxemia of pregnancy, J. A. M. A. 107: 1036-1040, 1936.

2. Addis, T., Blood pressure and pulse rate reaction, Arch. Int. Med. 30: 240-268, 1922.

3. Adson, A. W., Craig, W. M., and Brown, G. E., Postural hypotension, Coll. papers, Mayo Clin. 27: 972, 1935.

4. Allen, E. V., and Magee, H. R., Orthostatic (postural) hypotension with syncope, M. Clin. North America 18: 585-595, 1934.

5. Alvarez, W. C., Blood pressure in fifteen thousand university freshmen, Arch. Int. Med. 32: 17, 1923.

6. Alvarez, W. C., Blood pressure in university freshmen and office patients, Arch. Int. Med. 26: 381, 1920.

7. Apel, Maria, Effect of short wave therapy on blood pressure, M. Rec. 144: 229-230, 1936.

8. Ashworth, O. O., Postural hypotension, Virginia M. Monthly 56: 260-262, 1929.

9. Auer, John, and Meltzer, S. J., The administration of epinephrine by intraspinal injections, J. A. M. A. 70: 70, 1918.

10. Barach, J. H., Arterial hypotension, Arch. Int. Med. 35: 151-161, 1925.

11. Barach, J. H., Defecient oxygenation in arterial hypotension, Atlantic M. J. 29: 747-748, 1926.

12. Barker, N. W., Postural hypotension, M. Clin. North America 16: 1301-1312, 1933.

13. Barker, N. W., and Coleman, J. H., Postural hypotension associated with arteriosclerosis, M. Clin. North America 15: 241-243, 1931.

14. Bayliss, W. M., Methods of raising a low arterial pressure, Proc. Roy. Soc., London, s. B. 89: 380-393, 1916.

15. Bayliss, W. M., Treatment of low blood pressure, Brit. Med. J. 2: 808, 1917.

16. Bedford, E. A., The epinephric content of the blood in conditions of low blood pressure and shock, Am. J. Physiol. 43: 235-255, 1917.

17. Bishop, L. F., Secondary low blood pressure of an insidious type, J. M. Soc. New Jersey 20: 93-94, 1923.

18. Blake, James, Experimental lowering of the blood pressure, Edinburgh M. & S. 51: 330-346, 1839.

19. Blalock, Alfred, Experimental shock, Arch. Surg. 20: 959-996, 1930.

20. Blalock, Alfred, Experimental shock, Arch. Surg. 22: 598-616, 1931.

21. Blalock, Alfred, Trauma to the intestines, Arch. Surg. 22: 314-327, 1931.

22. Bradbury, Samuel, and Eggleston, Cary, Postural hypotension, Am. Heart J. 1: 73-86, 1926.

23. Bradbury, Samuel, and Eggleston, Cary, Postural hypotension, Am. Heart J. 3: 105-106, 1927.

24. Brams, W. A., Katz, N., and Kohn, L., The effect of abdominal distension and release on the blood pressure in the arteries and veins, Am. J. Physiol. 104: 120-126, 1933.

25. Brockington, C. F., Diphtheritic hypopiesia, Lancet 1: 1387-1390, 1931.

26. Brown. G. E., Clinical tests of function of the autonomic nervous system, J. A. M. A. 106: 353-357, 1936.

27. Burch, J. C., and Harrison, T. R., The effect of the administration of fluids on the fall in blood pressure caused by spinal anesthesia, Arch. Surg. 22: 1045-1046, 1931.

28. Burton-Opitz, R., The clinical significance of high and low blood pressure, J. M. Soc. New Jersey 28: 302-304, 1931.

29. Cadbury, W. W., The blood pressure of normal Cantonese students, Arch. Int. Med. 30: 362, 1922.

30. Chamberlain, E. N., The treatment of low blood pressure, Lancet 1: 889-890, 1929.

31. Cheney, Garnett, Sporadic trichinosis with extreme hypotension,

J. A. M. A. 86: 1004, 1926.

32. Chew, E. M., Allen, E. V., and Barker, N. W., Orthostatic hypotension, Northwest Med. 35: 297-303, 1936.

33. Cobb, Stanley, The cerebral circulation, Ann. Int. Med. 7: 292-302, 1933.

34. Code, C. F., and Dingle, W. T., The carotid sinus nerve, Proc. Staff Meet., Mayo Clin. 10: 129-132, 1935.

35. Cornwall, E. E., Low blood pressure, New York State J. Med. 99: 470-475, 1914.

36. Crampton, C. W., Blood ptosis, New York State J. Med. 98: 916-918, 1913.

37. Croll, F. W., Duthie, R. J., and McWilliams, J. A., Postural hypotension, Lancet 1: 194-198, 1935.

38. Crouch, H. T., Hypotension, Kentucky M. J. 25: 372-373, 1927.

39. Davis, N. S., Some observations on the etiology and treatment of pathological blood pressures, Illinois M. J. 51: 38-43, 1927.

40. Dearborn, G. V. N., Low arterial tension, M. & S. J. 181: 659-663, 1919.

41. Dessler, A. L., A case of eclampsia with relatively low blood pressure, Am. J. Obst. & Gynec. 13: 647-648, 1927.

42. Domonech-Alsina, F., Studies on histamine hypotension, J. Physiol. 78: 54-64, 1933.

43. Edgecombe, W., Some observations on low blood pressure, Practitioner 86: 515-536, 1911.

44. Ellis, M. M., Pulse rate and blood pressure responses of men to passive postural changes, Am. J. M. Sc. 161: 568-578, 1921.

45. Emerson, Haven, Blood pressure in tuberculosis, Arch. Int. Med. 7: 441-467, 1911

46. Erlanger, Joseph, and Hooker, D. R., An experimental study of blood pressure and of pulse pressure in man, Man. J. Hopkins Hosp. Report 12: 145-378, 1904.

47. Evans, T. S., Azotemia with normal kidneys found at post-mortem, Arch. Int. Med. 48: 1231, 1931.

48. Faught, F. A., Hypotension—its clinical significance, Interstate M. J. 19: 950-957, 1912.

49. Ferrannini, Andrea, Constitutional angiohypotony, Lancet 1: 1131-1132, 1931.

50. Ferrannini, Andrea, Constitutional angiohypotony, M. J. & Rec. 135: 381, 1932.

51. Fleming, H. W., and Naffziger, H. C., Physiology and treatment of transient hemiplegia, J. A. M. A. 89: 1484-1487, 1927.

52. Fossier, A. E., A cause of essential hypotension, Am. J. M. Sc. 171: 496-504, 1926.

53. Freeman, H., The blood pressure in schizophrenia, Arch. Neurol. & Psychiat. 27: 333-351, 1932.

54. Freeman, H., Effect of "habituation" on blood pressure in schizophrenia, Arch. Neurol. & Psychiat. 29: 139-147, 1933.

55. Friedlander, Alfred, Clinical types of hypotension, J. A. M. A. 83: 167-171, 1924.

56. Gaddum, J. H., and Schild, H., Depressor substances in extracts of intestine, J. Physiol. 83: 1-14, 1935.

57. Garvin, J. D., Hypotension, J. A. M. A. 88: 1875-1876, 1927.

58. Ghrist, D. G., Postural hypotension, Proc. Staff Meet., Mayo Clin. 2: 117-118, 1927.

59. Ghrist, D. G., and Brown, G. E., Postural hypotension with syncope, Am. J. M. Sc. 175: 336-349, 1928.

60. Ghrist, D. G., Variation in pulse and blood pressure with interrupted change of posture, Proc. Staff Meet., Mayo Clin, 5: 272-274, 1930.

61. Ghrist, D. G., Variation in pulse and blood pressure with interrupted change of posture, Ann. Int. Med. 4: 945-958, 1931.

62. Goodman, E. H., Some cases of hypotension associated with a definite symptomatology, Am. J. M. Sc. 147: 503-514, 1914.

63. Graham-Stewart, A., Observations on the significance of low

arterial pressures, Practitioner 120: 111-119, 1928.

64. Greaves, A. V., Low systolic blood pressure, Canad. M. A. J. 15: 174-177, 1925.

65. Hamon, P. H., and Harkins, H. N., Depressor substances in peritonitis, Proc. Soc. Exper. Biol. & Med. 32: 6-8, 1934.

66. Hay, John, The treatment of patients with abnormal blood pressure, Practitioner 136: 669-678, 1936.

67. Holt, Evelyn, Arterial hypotension, M.Clin. North America 19: 865-871, 1935.

68. Houghton, H. A., Arterial hypotension: a study in etiology and classification, M. & S. Year Book 1:237-250, 1929.

69. Hoxie, G. H., Endocrine therapy in cases of low blood pressure, Endocrinology 5: 773-776, 1921.

70. Hoxie, G. H., The clinical significance of low blood pressure, J. Missouri M. A. 18: 113-115, 1921.

71. Hoyle, Clifford, The treatment of high and low blood pressure, Practitioner 133: 442-444, 1934.

72. Hughes, T. A., and Yusaf, Mohammad, Postural hypotension, Lancet 1: 1101-1102, 1935.

73. Hunt, Reid, The fall of blood pressure resulting from the stimulation of afferent nerves, J. Physiol. 18: 381-410, 1895.

74. Johnson, W. M., Low blood pressure, South. Med. & Surg. 89: 1-5, 1927.

75. Kirby, D. W., Hypotension, J. Am. Inst. Homeop. 24: 1066-1071, 1931.

76. Laurens, Henry, Effect of carbon arc radiation on blood pressure and cardiac output, Arch. Phys. Therapy 17: 199-205, 1936.

77. Lawrence, C. H., Some aspects of hypotension, Interstate M. J. 23: 165-169, 1916.

78. Levison, L. A., The significance of arterial hypotension, Ohio State M. J. 20: 556-563, 1924.

79. McCrae, Thomas, Low blood pressure, M. Clin. North America 3: 1177-1195, 1920.

80. McQuiston, J. S., The relationship of arterial hypotension to surgical risk, J. Iowa M. Soc. 25: 331-333, 1935.

81. Martin, E. G., and Stiles, P. G., Two types of reflex fall of blood pressure, Am. J. Physiol. 34: 106-113, 1914.

82. Mayer, H. N., The blood ptosis test as a measure of physical efficiency, Railway Surg. J. 23: 179-183, 1917.

83. Mazzola, V. P., and Torrey, M. A., An experimental study of the effects of intravenous injections of hypertonic glucose solution (50%) on the circulation of the cat, Am. J. Obst. & Gynec. 30: 339-345, 1935.

84. Meakins, Jonathon, Arterial hypertension and hypotension and their clinical significance, Physiol. Rev. 7: 431-497, 1927.

85. Meakins, J. C., Jaundice and blood pressure, M. Clin. North America 16: 715-729, 1932.

86. Meltzer, S. J., and Salant, William, The effects of intravenous injections of bile upon blood pressure, J. Exper. Med. 7: 280-291, 1905.

87. Miller, T. G., Ephedrine: its use in the treatment of vascular hypotension and bronchial asthma Ann. Clin. Med. 4: 713-721, 1926.

88. Miller, T. G., The treatment of low blood pressure, Atlantic M. J. 29: 748-752, 1926.

89. Mortensen, M. A., Blood pressure reactions to passive postural changes an index to myocardial efficiency, Am. J. M. Sc. 165: 667-675, 1923.

90. Mortensen, M. A., Arterial hypotension, J. Michigan M. Soc. 30: 616-619, 1931.

91. Novarro, A., Pulsus alterans with hypotension, J. A. M. A. 83: 1721, 1924.

92. Osborne, W. A., Low blood pressure and secretory activity, Australian J. Exper. Biol. & M. Sc. 5: 171-172, 1928.

93. Pal, J., Low blood pressure, J. A. M. A. 81: 81, 1923.

94. Pal, J., Hypertension and hypotension--hypertonia and hypotonia, Internat. Clin. 4: 151-157, 1926.

95. Pearce, R. M., and Eisenbrey, A. B., A study of experimental conditions of low blood pressure of non-traumatic origin, Arch. Int. Med. 6: 218-230, 1910.

96. Pearce, R. M., and Eisenbrey, A. B., A study of experimental conditions of low blood pressure of non-traumatic origin, Tr. A. Am. Physicians 25: 30-44, 1910.

97. Pepper, O.H.P., Hypotension, Northwest Med. 34: 325-329, 1935.

98. Pepper, O.H.P., Hypotension, Northwest Med. 34: 380-384, 1935.

99. Pepper, O.H.P., Transient hypotension as a factor in cerebral thrombosis, Ann. Surg. 101: 296-302, 1935.

100. Phemister, D. B., and Livingstoh, H., Primary shock, Ann. Surg. 100: 714-727, 1934.

101. Pike, F. H. and Coombs, H. C., The relation of low blood pressure to a fatal termination in traumatic shock, J. A. M. A. 68: 1892-1893, 1917.

102. Potter, N. B., Some clinical examples of low and lowered systolic blood pressure, Internat. Clin. 4: 33-61, 1915.

103. Reicker, H. H., and Upjohn, E. G., Postural hypotension, Am. Heart J. 6: 225-229, 1930.

104. Roberts, S. R., A study of hypotension, J. A. M. A. 79: 262-268, 1922.

105. Rogoff, J. M., The adrenal medulla, J. A. M. A. 104: 2088-2092, 1935.

106. Roome, N. W., Keith, W. S., and Phemister, D. B., Experimental shock: the effect of bleeding after reduction of the blood pressure by various methods, Surg., Gynec. and Obst. 56: 161-168, 1933.

107. Sanders, A. O., Postural hypotension, Am. J. M. Sc. 182: 217-221, 1931.

108. Sanders, A. O., Postural hypotension, Am. Heart J. 7: 808-813, 1932.

109.Shambaugh, Philip, Azotemia due to low blood pressure, Arch, Int. Med. 50: 921-925, 1932.

110.Simond, J. P., A study of low blood pressure not associated with trauma or hemorrhage, Arch. Int. Med. 18: 848-855, 1916.

111.Simond, J. P., A study of low blood pressure associated with peptone shock and experimental fat embolism, J. A. M. A. 69: 883-884, 1917.

112.Stengel, Alfred, The clinical significance of arterial hypotension, Atlantic M. J. 29: 744-747, 1926.

113.Sutton, D. C., and Leuth, H. C., The treatment of hypotension in arteriosclerosis, Illinois M. J. 65: 500-502, 1934.

114.Symonds, Brandreth, The blood pressure of healthy men and women, J. A. M. A. 80: 232-236, 1923.

115.Tung, C. L., Relative hypotension of foreigners in China, Arch. Int. Med. 40: 153-158, 1927.

116.Vaughan, W. T., and Graham, W. R., Hypotension in the south, South. M. J. 23: 1140-1146, 1930.

117.Walker, J. B., Intravenous injection of hypertonic sodium chloride solution in the treatment of some contions of low blood pressure, Brit. J. Surg. 24: 105-121, 1936.

118.Weis, C. R., Postural hypotension with syncope, Ann. Int. Med. 8: 920-922, 1935.

119.Weiss, Soma, and Ellis, L. B., Treatment of arterial hypotension, Arch. Int. Med. 52: 105-119, 1933.

120.Williams, P. F., The significance of low blood pressure in pregnancy, Am. J. Obst. & Gynec. 18: 546-555, 1929.

121.Williams, P. F., The significance of low arterial pressure in pregnancy, Tr. Am. Gynec. Soc. 54: 153-154, 1930.

122.Wilson, Harwell, and Roome, N. W., The effect of constriction and release of an extremity, Arch Surg. 32: 334-345, 1936.

123.Wolfson, W. L., and Teller, Frank, The intravenous use of gelatine solution in hemorrhage, Am. J. M. Sc. 178: 562-

568, 1929.

124.Woltman, H. W., Postural hypotension, Proc. Staff Meet., Mayo Clin. 9: 541-545, 1934.