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During the past twenty years it has become increasingly apparent that one of the greatest dangers in the conduct of general anesthesia is the production of excessively deep anesthesia for the attainment of satisfactory muscular relaxation. Contrary to the antiquated and erroneous concept that general anesthesia resembles "physiologic sleep", it has become evident that such levels of general anesthesia are accompanied by untoward physiologic depression of the cardiovascular, pulmonary, and hepatorenal systems.

As early as 1930, techniques designed to circumvent these dangerous side effects were developed. An example of such an approach was the employment of spinal or conduction analgesia in combination with light general anesthesia. Though such techniques offered some improvement in safety for the patient, they were by no means ideal.

Not until 1942, when Richard Gill\textsuperscript{1} introduced curare, was real progress made toward the goal of providing adequate surgical anesthesia without serious physiologic depression. Unfortunately, the demand for such a product was so urgent that widespread clinical use ensued before a thorough knowledge of all its pharmacologic properties was understood. As with other long awaited, urgently needed products, curare became the victim of premature, injudicious usage. It was inevitable, therefore, that its introduction was soon followed by an era of rejection based on the conclusion that the agent possessed inherent toxic properties.\textsuperscript{2}

Then followed an era of critical scientific reevaluation by chemists and pharmacologists. New compounds possessing fewer side effects were synthesized and detailed studies of their pharmacologic actions

\textsuperscript{1}This is an address given at the Staff Meeting of the University of Minnesota Hospitals on November 16, 1956.

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THE MEDICAL BULLETIN

enumerated. Carefully controlled clinical evaluations were carried out by qualified anesthesiologists.

This sorely needed reappraisal led to the formulation of new concepts of application of these valuable agents. Hazards, indications, and limitations were recognized and more intelligent usage fostered.

The culmination of these studies was reached at the World Congress of Anesthesiologists in Scheveningen in September, 1955, when representatives of 39 nations acclaimed the introduction of muscle relaxants to be one of three great advances of anesthesia during the past quarter century.

It is the purpose of this paper to consider the current status of the muscle relaxants.

Pharmacology:

A. Neuromuscular transmission. To understand the properties of the muscle relaxants, normal neuromuscular transmission must be reviewed briefly. Following stimulation of a motor nerve acetylcholine is released at the motor end plate. This attaches to receptors on the post-junctional membrane and depolarizes it, initiating muscular contraction. Acetylcholinesterase and plasma pseudocholinesterase rapidly hydrolyze acetylcholine to acetic acid and choline, the post-junctional membrane repolarizes and is ready for the next impulse.

B. Mode of action of muscle relaxants. Skeletal muscle relaxants block neuromuscular transmission in two ways: (1) they lessen the effectiveness of acetylcholine by competing for the receptors on the post-junctional membrane, thus preventing depolarization, or (2) they produce a persistent depolarization of the post-junctional membrane which prevents repolarization and, therefore, blocks transmission.

C. Classification of muscle relaxants. The classification of muscle relaxants is based on the mode of action by which they block neuromuscular transmission. They are divided into three types. Type one, the competitive neuromuscular blocking agents, includes curare, d-tubocurarine, dimethyl tubocurarine chloride (Mecostrin®), dimethyl tubocurarine iodide (Metubine®), gallamine triethiodide (Flaxedil®), and erythrin alkaloids. Type two, the depolarization blocking agents, includes decamethonium (Syncurine®) and succinylcholine chloride (Anectine®). Type three, the mixed blocking agents, is exemplified by benzoquinonium (Mytolon®).

Of the compounds in the foregoing classification, d-tubocurarine,
gallamine triethiodide, decamethonium and succinylcholine are used most extensively; therefore, the discussion in this paper will be limited to these drugs. The pharmacologic properties of these relaxants are shown in Table I.

### TABLE 1

PROPERTIES OF MUSCLE RELAXANTS

<table>
<thead>
<tr>
<th>Properties</th>
<th>d-Tubocurarine</th>
<th>Gallamine Triethiodide</th>
<th>Succinylcholine</th>
<th>Decamethonium</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Effect on CNS</td>
<td>None in doses 3-4 times normal clinical doses</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>2. Effect on cardiovascular system</td>
<td>Slight fall in blood pressure</td>
<td>Slight increase in blood pressure and pulse</td>
<td>Slight increase in pulse rate</td>
<td>Slight increase in pulse rate</td>
</tr>
<tr>
<td>3. Effect on respiratory system</td>
<td>Depressed tidal volume to complete respiratory muscle paralysis</td>
<td>Same</td>
<td>Same</td>
<td>Same</td>
</tr>
<tr>
<td>4. Effect on skeletal muscle</td>
<td>Relaxation, competitive block</td>
<td>Same, competitive block</td>
<td>Same, depolarization block</td>
<td>Same, depolarization block</td>
</tr>
<tr>
<td>5. Effect on autonomic ganglion</td>
<td>Blocks mildly in clinical doses</td>
<td>Very minimal, if any</td>
<td>No effect</td>
<td>No effect</td>
</tr>
<tr>
<td>6. Effect on kidneys and liver</td>
<td>No effect</td>
<td>No effect</td>
<td>No effect</td>
<td>No effect</td>
</tr>
<tr>
<td>7. Histamine release</td>
<td>Marked</td>
<td>Minimal</td>
<td>Not significant</td>
<td>Not significant</td>
</tr>
<tr>
<td>8. Excretion</td>
<td>Partially detoxified in liver, excreted by kidney</td>
<td>By kidney</td>
<td>Hydrolyzed by plasma pseudocholinesterase, by-products excreted by kidney</td>
<td>By kidney</td>
</tr>
<tr>
<td>9. Antagonists</td>
<td>Neostigmine, edrophonium</td>
<td>Neostigmine, edrophonium</td>
<td>Fresh whole blood</td>
<td>None</td>
</tr>
<tr>
<td>10. Tachyphylaxis</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**D-Tubocurarine**

As noted in the chart, d-tubocurarine may cause a fall in blood pressure after intravenous administration. This is most pronounced if the drug is given rapidly in large doses. The hypotensive response is the result of three physiologic alterations, decreased muscular tone, autonomic ganglionic blockade, and histamine release.

It should be noted that the other relaxants do not share the latter two properties to any significant degree. Even d-tubocurarine produces only a minimal degree of ganglionic blockade in therapeutic doses, and the release of significant quantities of histamine occurs only in allergic patients. The hypotensive property of d-tubocurarine does not
necessarily preclude its use since in most instances the blood pressure will return to normal without therapy in a period of minutes. In the rare case where blood pressure does not return to normal the judicious use of a peripherally acting vasopressor will correct the hypotension.

D-tubocurarine depends upon the liver for partial detoxification. The remainder of the drug and its by-products are excreted by the kidneys. Its action is readily antagonized by neostigmine and edrophonium.

Gallamine Triethiodide (Flaxedil®)

A unique property of gallamine is its inhibitory or atropine-like effect on the cardiac vagus nerve. This action is protective against cardiac reflexes mediated through this nerve. In addition, flaxedil depresses the hydrocarbon sensitization of the myocardium to epinephrine. The cardio-accelerating effect of flaxedil accounts for an increase in cardiac output and elevation of arterial pressure. There are instances when tachycardia may be considered undesirable and this drug should be avoided. Flaxedil has minimal visceral autonomic ganglion blocking properties and the histamine released after intravenous administration is insignificant.

Flaxedil does not depend upon the liver for its detoxification. It is excreted unchanged by the kidneys. Like d-tubocurarine, it is antagonized readily by neostigmine and edrophonium.

Succinyldicholine

Succinyldicholine has a rapid onset and short duration of action. It is rapidly hydrolyzed by plasma pseudocholinesterase into succinylmonocholine and choline. Succinylmonocholine also has neuromuscular blocking properties. It is 25 times weaker than the parent substance but hydrolysis is much slower. If large doses of succinyldicholine are used, prolongation of neuromuscular block as a result of accumulation of succinylmonocholine, may be observed. It may be antagonized by fresh whole blood because of its pseudocholinesterase content. Cholase®, a pseudocholinesterase, has received enthusiastic acclaim in England as an antagonist of succinyldicholine. The end products of hydrolysis are excreted in the urine. Succinylmonocholine is readily antagonized by edrophonium.

Decamethonium

Decamethonium, also a depolarization blocker, has the undesirable properties of tachyphylaxis, variability of action, and lack of an antagonist. Spencer and Coakley point out that the variability of action from
patient to patient may be troublesome. They state the drug appears to be less potent in alcoholics and in patients habituated to barbiturates, paraldehyde, or other hypnotics. The drug does not produce undesirable effects on the cardiovascular system, and histamine release is minimal. Decamethonium is excreted unchanged in the urine.

*Indications and Uses*

The indications and correct usage of any group of drugs ultimately are predicted upon a thorough understanding of their pharmacologic and physiologic effects, upon the laboratory and clinical experience gained with them, and upon the advantages and disadvantages which these factors present to the extant circumstances. It is reasonable to feel that sufficient information of the muscle relaxants is available today, and that a list of indications can be presented properly.

The primary indication for the use of muscle relaxants is found in their ability to provide excellent surgical conditions without the need for deep general anesthesia. This indication assumes greater significance in the poor risk patient in whom deep general anesthesia is especially hazardous.

A second indication for the use of relaxants is the necessity for a smooth induction phase. Straining, coughing, bucking, and breath holding, while common in inhalation anesthesia, are minimized or abolished when relaxants are employed. Such management is particularly beneficial to the patient with severe cardiac, respiratory, or central nervous system disease.

A third advantage is represented in the improvement in exposure, accessibility, and tranquility of the surgical field. These conditions greatly facilitate the accomplishment of delicate surgical procedures without undue anesthetic depression.

The fourth outstanding indication seldom is appreciated by those who have not experienced an anesthetic explosion. The efficacy of combining a muscle relaxant with non-explosive, but weak anesthetic gases, sedatives, and hypnotic drugs in producing adequate operative conditions leaves very few indications for the use of explosive gases and vapors.

Fifth, the muscle relaxants are indicated therapeutically to interrupt laryngospasm and the convulsions of tetanus and status epilepticus and to protect against the convulsions associated with electro-shock therapy.
Contraindications to the Use of Relaxants

There are no absolute contraindications to the use of relaxants when considered as a group, but definite contraindications to use of each individual relaxant have been identified. Some of these conditions completely prohibit the use of one of the relaxants but may allow safe usage of one or more of the allied agents.

A. Myasthenia gravis. The use of d-tubocurarine, gallamine and other non-depolarizing blockers, in the presence of myasthenia gravis is hazardous since marked exaggeration and prolongation of the muscular flaccidity may be produced. Decamethonium and succinylcholine may be used safely in the presence of this disease. In some instances, the patient may be refractory to the latter two drugs.

B. Intestinal obstruction. The use of relaxants may prove hazardous in patients with intestinal obstruction because of two major factors. The distended, fluid-filled stomach and intestines impose constantly the danger of regurgitation and aspiration of intestinal contents, despite apparently adequate drainage through a stomach tube. It is imperative in this instance that a cuffed endotracheal tube be inserted under topical anesthesia before any general anesthetic agent or relaxant is administered. In patients with protracted intestinal obstruction, dehydration, electrolyte imbalance, and low urinary output are common findings. Under these circumstances the relaxants may exert prolonged effects, due to altered ionic conditions at the myoneural junction and because of impaired renal excretion. Under such conditions the avoidance of the muscle relaxants is recommended.

C. Airway obstruction. In patients exhibiting airway obstruction as a result of tumors of the thyroid gland, larynx, or oropharynx, relaxants must be used with extreme caution. The reduction of muscular tone by the relaxant may cause critical impairment of the patient's ability to maintain a patent airway. One is then obligated to establish an adequate airway by mechanical means which, in certain instances, may be extremely difficult and occasionally impossible.

D. Allergic states. In patients known to exhibit allergic reactions and in particular those with bronchial asthma, d-tubocurarine should be avoided because of its property of histamine production, which may precipitate bronchospasm and severe hypotension. Gallamine, succinylcholine, or decamethonium may be employed safely since no significant histamine release accompanies their use.

E. Hemorrhagic shock. In shock due to hypovolemia, there is an in-
creased hazard associated with the use of muscle relaxants. As pointed out above, the reduction of muscle tone and ganglionic blockade may aggravate the hypotension. In addition, the impairment of hepatic and renal function commonly present in shock may render the action of the relaxants unduely prolonged.

F. Heart disease. The benefits gained by the cardiac patient since the advent of the muscle relaxants are several. Induction of anesthesia is smooth, swift and unaccompanied by coughing, straining, struggling or hypoxia. Prolonged anesthesia in a light plane with minimal depression of the damaged heart can be assured; however, precautions must be taken to safeguard the patient with heart disease against certain side effects of the relaxants. D-tubocurarine should be avoided in such patients because of its tendency to produce hypotension. Gallamine is ideal for the cardiac patient unless the mild tachycardia which it produces occasionally is considered especially hazardous. Succinyldicholine, except in very large doses, has no cardiovascular effect and is well tolerated by the damaged heart.  

G. Renal disease. It has been implied already that the presence of significant renal disease militates against the use of relaxants which are excreted in the urine. D-tubocurarine, though partially detoxified by the liver, may exert prolonged effects when administered in the presence of depressed renal function. Likewise, gallamine and decamethonium which depend totally on the renal route for excretion, are hazardous under these circumstances. Succinyldicholine is the agent of choice since its detoxification occurs by enzymatic hydrolysis.

H. Liver disease. Cirrhosis, hepatitis, severe malnutrition and cachexia are associated with depressed hepatic function. Accordingly, the administration of d-tubocurarine may result in prolonged action of the drug. Similarly, since the liver is the source of the plasma enzyme, pseudocholinesterase, and since this product is essential for the hydrolysis of succinyldicholine, this drug should not be employed in the presence of liver disease. Gallamine used judiciously, in recognition of the well-known sensitivity of such debilitated patients to all drugs, is the most satisfactory relaxant in such cases.

I. Glaucoma. Since succinyldicholine may cause sustained elevation of the intraocular pressure it should be avoided in glaucoma.

J. Ether Anesthesia. Ether has a competitive blocking effect similar to that of d-tubocurarine and gallamine upon the myoneural junction. Potentiation and prolongation of the response to the latter drugs is
possible in the presence of ether. Succinylidicholine may be used safely with ether because it is a depolarizing compound and also is hydrolyzed quickly.

K. Procaine anesthesia. Both succinylidicholine and procaine are hydrolyzed by plasma pseudocholinesterase, compete for this enzyme system, and thus produce an effect similar to potentiation when used simultaneously.

Management of Respiratory Paralysis

Because paralysis of the muscles of respiration is a property common to all relaxants, the most serious complications seen following their use are the result of inadequate management of depressed ventilation.

Assisted respiration is the primary need of the patient with reduced tidal volume. It is mandatory that the muscle relaxants be used only by individuals adequately trained to maintain the airway and to provide physiological artificial ventilation. In conjunction with these methods, the pharmacologic antagonists may be employed to hasten the termination of the effects of the muscle relaxants.

Those who have ignored these cardinal principles have contributed unduly to the literature upon which the original condemnation of the relaxants was based.

REFERENCES


Small Vessel Changes in Femoral Arteriography*

Alexander R. Margulis, M.D., and T. O. Murphy, M.D.

The interest in peripheral arteriography is almost as old as the field of roentgenology, itself. In 1896 a short time after the publication of Roentgen's discovery, Haschek and Lindenthal injected and demonstrated the arteries of an amputated hand. In spite of many attempts to devise a safe method to demonstrate the vessels in viable tissue, arteriography remained a tool of research in animals until 1923 when Berberich and Hirsch performed the first angiogram in a living human being using strontium bromide. There followed a search for the ideal contrast medium. As outlined by Edwards, such a medium must be safe, nonirritating in the vessel or when extravasated, chemically stable, non-allergenic, easily handled, freely flowing, miscible with the blood, and without danger of embolization. Above all, it must be quite radiopaque. There is no medium available at present that satisfies all these criteria. Contrast materials in current use represent a great improvement over the early substances and have made femoral arteriography a safe procedure of great diagnostic value, which can be used in the majority of patients.

Most of the interest in femoral arteriography has been centered on the study of rather gross arterial changes and the demonstration of obstructions in large vessels. Stimulated by the success of various vascular reconstitution operations, an interest and need has developed to know more about the vascular bed beyond the patency of large vessels. If a bypass arterial graft is to remain open and supply blood to the distal capillaries, the status of small vessels and the site and abundance of collaterals are essential information. As the scope of such surgery advances and the procedures become more extensive, the amount of information that the vascular surgeon demands increases. Attention to detail and painstaking search for changes in the small vessels thus assume practical importance and transcend mere academic interest.

*This is an address given at the Staff Meeting of the University of Minnesota Hospitals on November 23, 1956.
1Assistant Professor, Department of Radiology.
2Instructor, Department of Surgery.
The purpose of this paper is to present and discuss several types of small vessel changes as demonstrated by femoral arteriography. These are only a few instances which are presented as examples. A whole new field of changes in small vessels in peripheral and systemic vascular disease is still uncharted. These studies are just incursions into the periphery of a wide, unexplored territory.

**Arteriovenous Communications**

Congenital or traumatic arteriovenous communications located in the deep tissues of the extremities are not difficult to diagnose clinically or from arteriograms. Massive amounts of blood are shunted through these fistulae, producing the symptoms and signs of large extracardiac left-to-right shunts. Locally the changes are also obvious. According to DeTakats, this type of arteriovenous communication, if congenital, is due to local arrest at the retiform stage of development of the vascular bed. This type of vascular abnormality is not common in the extremities.

Small peripheral congenital arteriovenous communications, even when numerous, present considerably more challenge in their diagnosis. Since the work of Hoyer in 1877 and later of Sucquet and Schumaker, it has been demonstrated that normal arteriovenous communications exist as well as abnormal ones. Lewis has shown that the normal arteriovenous communications located in the skin, the glomus bodies of Masson, are important in the thermoregulatory mechanism. Popoff has shown that some of these glomus units can develop abnormally with a failure of neuromuscular control. The lumen of these units is usually large and may be in excess of 0.1 mm. in diameter. It is quite evident, therefore, that if many such maldeveloped units are present a potentially massive shunt can result. Since the basic unit of this type of shunt is so anatomically small and the effects additive, the diagnosis is difficult both from the standpoint of being aware of the presence of the condition and from the standpoint of localizing the exact site of shunt. In this hospital we have studied nine patients with surgically proven congenital superficial arteriovenous communications. The almost simultaneous demonstration of superficial veins and arteries is a diagnostic feature of this type of malformation. Simultaneous demonstration of superficial and deep veins with major arteries is an indication of a massive shunt. While these signs are diagnostic they do not demonstrate the exact area in which the shunting occurs but are a graphic demonstration of the summation effect of the multiple communications.
Three additional signs in which smaller vessels are demonstrated are helpful in establishing the diagnosis of this condition.

a. The venous rete is a small or large formation of arterialized veins carrying arterial blood. These veins have thickened walls, and when visualized at operation are seen to pulsate. Massive retia have been demonstrated around the ankle, the knee, and occasionally elsewhere. Small, isolated rete formations are not uncommon. Frequently, apparently normal individuals will have a few isolated rete formations. Since only a small shunt results no symptoms will ensue.

b. The “H” formation is a group of vessels which we have encountered in all nine patients with surgically proved congenital arteriovenous communications. It consists of a vessel lying parallel to the deep artery and connected with it by means of a small vessel. The latter usually enters the parallel vessel at an angle close to 90 degrees. Even more frequently than the venous rete, the “H” formation may be seen in apparently normal individuals. Multiplicity and prominence of this sign, however, was encountered only in congenital arteriovenous communications. When seen at operation the parallel limb of the “H” formation is a small vein carrying arterial blood, pulsating and showing histologic changes secondary to the shunt. In one of the studies, multiple “H” formations were the only prominent features of the arteriogram enabling the radiologist to make the diagnosis without the benefit of any clinical information. We believe that the “H” formation is the demonstration of the communication itself. The presence of normal arteriovenous bypasses which are under neuromuscular control has been well established. In postmortem injection studies after the neuromuscular control had been eliminated multiple “H” formations have been observed.

c. Segmentation.

The anatomical dissection of specimens shows multiple small branches coming off major vessels. Muscular, articular, and nutrient vessels supplying bone can quite easily be identified. The normal arteriogram usually does not show these branches. Only the larger branches of the major vessels are seen. In instances of superficial congenital arteriovenous communications, due to increased flow of blood in the subcutaneous tissues, the hydrodynamic relations of small vessels are changed. There are dilated small arteries which carry large amounts of blood to the peripheral shunts, and thus they are visualized coming off at regular intervals from the major deep vessels in the
regions of involvement. This was seen in seven of nine cases (Table I).

While the diagnosis of superficial congenital arteriovenous communications can be made from arteriograms without much difficulty, their surgical treatment at present rarely offers definite and lasting success. Ligation of the multiple feeding arteries will eliminate the effects of the abnormality for some time, but recurrence is quite common. Signs of arteriovenous communications demonstrable both clinically and by arteriography frequently occur in the very area where ligations have been performed previously. Whether new arteriovenous communications develop or whether small ones that were already present dilate and carry large amounts of blood is a question of debate. The latter appears to be the more likely explanation.

Acquired Arteriovenous Fistulae

Trauma is by far the most frequent cause of acquired arteriovenous fistulae. Yater et al. have reported a mycotic arteriovenous fistula, and occasionally arteriosclerotic aneurysms will develop into an arteriovenous communication. Their detection is not difficult. Lewis has shown that an arteriovenous communication acts as a short circuit and the blood supply to the tissues distal to the fistula is diminished. If the fistula persists long enough, however, the blood flow to the tissues distal to the communication increases. Most descriptions in the past have stressed the demonstration by arteriography of large veins leading away from the site of the fistula. Allen, Barker and Hines however, pointed out the fact that while this is true in small communications,

<table>
<thead>
<tr>
<th>TABLE I</th>
<th>ROENTGEN SIGNS OF CONGENITAL ARTERIOVENOUS COMMUNICATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nine Cases</td>
<td></td>
</tr>
<tr>
<td>Simultaneous demonstration of deep venous channels</td>
<td>1</td>
</tr>
<tr>
<td>Simultaneous demonstration of superficial venous channels</td>
<td>8</td>
</tr>
<tr>
<td>Venous rete</td>
<td>8</td>
</tr>
<tr>
<td>&quot;H&quot; Formations</td>
<td>9</td>
</tr>
<tr>
<td>Prominent segmentation</td>
<td>7</td>
</tr>
<tr>
<td>Non-tapering of peripheral vessels</td>
<td>9</td>
</tr>
</tbody>
</table>

with large fistulae, veins distal to the site of communication are visible, dilated and tortuous. We have seen increased flow and multiple arteriovenous communications, demonstrable by arteriography, distal to the site of the obvious acquired communication. On histologic section arterialized veins are seen distally and in arteriograms venous retia similar to those observed in congenital arteriovenous communications can be shown.

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Arteriography can be of great practical value in the diagnosis of tumors of bone and soft tissues. The classic paper of Dos Santos illustrated that point with brilliant examples. The value of arteriography has also been presented by Mucchi and Collumella and by Sutton. The method has great value. It affords the possibility of differentiating inflammatory processes and tumors, a problem which is not frequently encountered. It permits a fairly accurate delineation of the tumor which is impossible to do by any other radiographic method. In addition, it allows, according to Dos Santos, an estimate of activity of growth by observing the rapidity of arteriovenous shunt in the tumor itself. Finally, the technical surgical problems of a vascular tumor are predictable.

The diagnosis of a malignant tumor in the extremity, either in the bone or in the soft tissues is made by observing a network of irregular vessels, branching in all directions and quite different from the surrounding normal tissues. Occasionally dilatations, "the blood pools", of Dos Santos, will be observed, especially in sarcomas. These abnormal vessels act as arteriovenous communications, and immediate visualization of deep veins leading away from the tumor is obtained. These findings are characteristic and are not seen in inflammatory lesions or benign tumors. In addition to the described signs, it is not infrequent to encounter avascular areas within a tumor, surrounded by the irregular network of vessels. These areas seem to correspond to the necrotic areas within a renal carcinoma, as demonstrated by abdominal aortography. Malignant bone tumors are relatively rare, and there are few series of sufficient magnitude of the various histologic types. If such series could be accumulated it is conceivable that a method approaching histologic accuracy, at least for larger subdivisions, could be devised. This will require tedious and meticulous studies but the advantage of having some such advance knowledge is obvious.

Small Vessel Changes Demonstrated by Arteriography in Peripheral Occlusive Vascular Disease

Occlusive peripheral vascular disease is the main application of femoral arteriography. In the past, however, most studies were directed toward discovering the site of occlusion. The decisions whether to operate and what operative procedure to undertake are not entirely dependent on the site of occlusion alone. The arteriogram should be studied to obtain information about the status, abundance, and site of
collaterals and about the status and appearance of the small vessels in general and in the area distal to the site of occlusion. Marked irregularity of the lumen and repeated areas of narrowing in branches may contribute to the general status of the distal circulation so greatly that their importance may overshadow the role of a major vessel occlusion.

**Collaterals**

In uncomplicated arteriosclerosis obliterans the collaterals are tortuous, do not taper, and are usually abundant. With occlusions in the thigh they follow a predictable pattern of flow (Table II). Collaterals developing to compensate for occlusions of the leg vessels follow an unpredictable pattern. It is important to observe the location of the most abundant collaterals and the deviations from the common pattern. The lateral circumflex femoris group of collaterals is usually the main bypass in occlusion of the superficial femoral artery. In an occasional case the medial group is the mainstay of the circulation. This is important information to the surgeon who must preserve collaterals. The importance of these collaterals is also brought out by the fact that asymptomatic occlusions of major vessels are relatively common.

In a study of 84 patients with occlusive peripheral vascular disease, collateral circulation was found to be poor in the majority of patients who had diabetes in addition to arteriosclerosis (Table III). Patients
with uncomplicated arteriosclerosis obliterans had the highest incidence of good collateral circulation in our group. This figure is to be interpreted in the light of the fact that all the patients in our group had symptoms of marked peripheral vascular impairment, and, therefore, the study was based on occlusive disease where the collaterals were not adequate.

**Clubbing**

A large number of the arteriograms carried out in patients with occlusive peripheral vascular disease showed sudden endings of small vessels, usually quite close to their origin. The ending of the small vessel quite frequently had a dilatation, and for this reason we gave it the descriptive name of clubbing. Table IV shows the incidence of clubbing in a series of 84 cases of symptomatic occlusive disease, as well as the correlation of clubbing with the disease associated with arteriosclerosis obliterans. The frequency of demonstration of clubbing

### TABLE III

<table>
<thead>
<tr>
<th>Status of Collaterals</th>
<th>No. of patients</th>
<th>Poor</th>
<th>Good</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>84</td>
<td>38</td>
<td>46</td>
</tr>
<tr>
<td>Arteriosclerosis obliterans</td>
<td>42</td>
<td>14</td>
<td>28</td>
</tr>
<tr>
<td>Diabetic</td>
<td>27</td>
<td>17</td>
<td>10</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>14</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Syphilitic</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
</tbody>
</table>

### TABLE IV

<table>
<thead>
<tr>
<th>Presence of Clubbing</th>
<th>Total patients</th>
<th>None</th>
<th>Rare</th>
<th>Frequent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic</td>
<td>27</td>
<td>1</td>
<td>11</td>
<td>15</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>14</td>
<td>1</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Arteriosclerosis obliterans</td>
<td>42</td>
<td>33</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Syphilitic</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
</tbody>
</table>

by arteriography is not a good indication of its actual distribution, as it is quite likely that in extremities with poor collaterals and in those where small vessel disease is most advanced, the clubbing is not demonstrated because the small vessels are occluded and do not fill. Although clubbing in our series was most commonly associated with diabetes and hypertension, we believe it to be a nonspecific manifestation of small vessel disease. It can be correlated histologically with endarterial intimal proliferation that is found in the same type of vessels and under the same conditions. In evaluating clubbing one should have the demonstration of the same structure in at least two consecutive films, in order to avoid the possibility that a chance appearance of a patent
vessel at the point that the contrast material has reached at the time of exposure will be mistaken for this condition. Serial arteriography is the best technique for studying clubbing.

**Microaneurysms**

In a large number of cases small outpouchings on the side of small vessels were demonstrable (Table V). The majority of these patients were diabetics. We have called these outpouchings microaneurysms due to their similarity to the microaneurysms observed in the fundus of the eye in diabetic retinopathy. Correlating the appearance with the known changes that can be studied experimentally, we believe that microaneurysms may be due to unilateral weakening of the media of small vessels involved.

In studying an arteriogram it is important to be able to see the outpouching completely separate from the side of the underlying vessel. On at least two separate exposures the microaneurysm should appear unchanged; no vessel should be seen to continue from it. These precautions are necessary in order to avoid confusion of microaneurysms with windings of tortuous vessels. We believe microaneurysms, like clubbing, are nonspecific manifestations of small vessel disease. In our experience, however, they are often associated with diabetes.

### Table V

**Presence of Microaneurysms**

<table>
<thead>
<tr>
<th></th>
<th>Total Patients</th>
<th>None</th>
<th>Rare</th>
<th>Frequent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic</td>
<td>(27)</td>
<td>0</td>
<td>6</td>
<td>21</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>(14)</td>
<td>2</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Arteriosclerosis obliterans</td>
<td>(42)</td>
<td>35</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Syphilitic</td>
<td>(1)</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Summary

The importance of small vessel changes in femoral arteriography has been discussed. Examples demonstrating the value of signs derived from the study of small vessels in arteriography have been given. Arteriovenous communications, bone and soft tissue tumors, as well as some small vessel changes in peripheral occlusive vascular disease have been described.
REFERENCES


Editorials

The Teaching of Science

An important activity of the Minnesota Science Teachers' Association deserves the attention and support of all physicians in our state. This Association has done an outstanding job in improving the teaching of the sciences in Minnesota high schools, and its program for attracting larger numbers of able people to this field appears to be promising.

A committee of the Association, the Business, Industry, and Teachers of Science Committee (BITS), is sponsoring a Science Teachers' Conference next spring on Friday, May 3, 1957. In order to make possible maximum attendance at the conference by high school teachers, BITS urges the professions and industry to help by making their members and scientists available as substitute or guest teachers in the various high schools on the day of the Conference. Thus, a physician might take over a biology or general science class, and a chemist or engineer a chemistry or physics class, freeing the teacher in each instance so that he might attend the Conference.

High school teachers themselves and members of the BITS Committee will communicate with members of the various professional groups concerning this program. Physicians who wish to volunteer their services for this purpose may do so by writing to the principal of their local high school or to Mr. Martin Thames, Bemidji High School, Bemidji, Minnesota, Secretary of BITS.

The physicians of our state are fully aware of the importance of good teaching of scientific subjects in the secondary schools. We are certain that they will welcome this opportunity to be of service in a small but significant way.

Staff Meeting Reports

The attention of our readers is invited to the fact that the staff meeting reports appearing in this issue of the BULLETIN are published in their entirety. They contain not only the tables appearing in the original manuscripts but references as well. We hope our readers will let us know whether they prefer this style or the abbreviated versions that have appeared in the past.
Medical School Activities

Student Organizations

Student organizations are of real importance to medical students and faculty alike. The scope of their interests and activities has increased significantly in recent years. In an earlier issue of the BULLETIN (Vol. 27, No. 7, p. 130, Feb. 1, 1956), the various organizations were described in some detail. It is appropriate at this time to name the responsible officers of these organizations for the current academic year.

Medical Students' Advisory Council
JOHN R. SHEFVELAND, President
JOHN W. POLLARD, Vice-President
RAYMOND G. ARMSTRONG, Secretary
WILLIAM N. SPELLACY, Treasurer

Student American Medical Association
WENDELL A. JOHNSON, President
GERALD E. NELSON, Secretary

Class Officers
Senior Class
JOHN R. SHEFVELAND, President
FRED A. LYON, Vice-President
JOHN W. POLLARD, Secretary
WILLIAM N. SPELLACY, President
WILFRED A. CORSON, Vice-President
JAMES HERBERG, Secretary

Junior Class
RONALD C. YOUNG, President
BRUCE H. WARREN, Vice-President
RAYMOND G. ARMSTRONG, Secretary
JAMES SWENSON, President
THOMAS JOHNSON, Vice-President
CONRAD WILKOWSKE, Secretary

Medical Fraternities and Sororities
Alpha Epsilon Iota
BARBARA A. ROSINE, President
SONJA K. MYHRE, Secretary
GERALD T. MULLIN, President
LEE A. SIMSO, Secretary

Alpha Kappa Kappa
RICHARD D. CUNNINGHAM, President
HERBERT S. STRAIT, Secretary
JOHN S. GLETNE, President
KENNETH HALVORSON, Secretary

Nu Sigma Nu
JOSEPH H. EUSTERMAN, President
DOUGLAS A. LOWE, Secretary
DAVID A. BERMANN, President
GERALD RATINOV, Secretary

Phi Rho Sigma
ANTON F. SPRAITZ, President
GEORGE E. JACKISH, Secretary

Phi Beta Pi
BARBARA A. ROSINE, President
SONJA K. MYHRE, Secretary

Phi Chi
RICHARD D. CUNNINGHAM, President
HERBERT S. STRAIT, Secretary
JOHN S. GLETNE, President
KENNETH HALVORSON, Secretary

Phi Delta Epsilon
JOSEPH H. EUSTERMAN, President
DOUGLAS A. LOWE, Secretary
DAVID A. BERMANN, President
GERALD RATINOV, Secretary
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Diabetes Detection Drive

DR. FREDERICK C. GOETZ, Instructor, Department of Medicine, served as chairman for the Twin City’s observance of Diabetes Detection Week held November 11 through 17. The program was part of a national program sponsored by the American Diabetes Association with the cooperation of local druggists associations.

For the first time, the University participated as a community in the diabetes detection and education program. DR. STELLA SIKKEMA, University Health Service physician, served as chairman of the campus program, with Sigma Epsilon Sigma, sophomore women’s honor sorority, serving as the sponsoring student organization.

Over 40,000 individual detection kits were distributed by local druggists in the Twin City area, and over 5,000 more were distributed to University students and staff. Test results will be mailed to individuals and a follow-up will be made on all people whose tests are positive. Blood sugar tests will be made through University Hospital laboratories in cases where a follow-up is indicated.

Faculty News

Nine members of the Faculty received grants for research in cardiovascular disease under the joint support program of the American Heart Association and the Minnesota Heart Association. Those receiving grants include DOCTORS ELLIS S. BENSON, Assistant Director of Hospital Laboratories, H. MEAD CAVERT, Assistant Professor of Physiology, RICHARD A. DE WALL, Surgery Research Assistant, ROBERT A. GOOD, Professor of Pediatrics, ANCEL KEYS, Professor and Director of the Laboratory of Physiological Hygiene, RICHARD T. SMITH, Assistant Professor of Pediatrics, HENRY L. TAYLOR, Associate Professor of the Laboratory of Physiological Hygiene, LOUIS TOBIAN, Associate Professor of Medicine, and RICHARD VON KORFF, Research Fellow in Pediatrics.

On September 11, DR. WENTWORTH QUAST, Instructor, Division of Neurology, presented a paper entitled “A Follow-up of Children Discharged from a Psychiatric Ward” to the Minnesota Society for Neurology and Psychiatry.
Postgraduate Education

Urology for General Physicians

The University of Minnesota announces a continuation course in Urology for General Physicians which will be held at the Center for Continuation Study from January 3 to 5, 1957. Management of the commonly met urological problems will be stressed. The program will be presented under the direction of DR. C. D. CREEVY, Professor and Director, Division of Urology. The faculty for the course will include members of the faculties of the University of Minnesota Medical School and the Mayo Foundation.

Dermatology for General Physicians

A continuation course in Dermatology for General Physicians will be presented by the University of Minnesota next January 7 to 9, 1957, at the Center for Continuation Study. Diagnosis and management of those skin disorders most frequently seen in general practice will be emphasized. Guest speaker will be DR. NORMAN F. CONANT, Professor of Mycology and Associate Professor of Bacteriology, Duke University School of Medicine, Durham, North Carolina. The course will be presented under the direction of DR. HENRY E. MICHELSO, Professor, Department of Medicine, and Director, Division of Dermatology, and the remainder of the faculty will be drawn from the faculties of the University of Minnesota Medical School and the Mayo Foundation.

Notice

All continuation courses presented by the University of Minnesota are approved for formal postgraduate credit by the American Academy of General Practice. Attendance certificates will be furnished on request. Further information concerning the above programs or others to be presented may be obtained by writing to Dr. Robert B. Howard, 1342 Mayo Memorial, University of Minnesota, Minneapolis 14.
Coming Events

December 3  HENNEPIN COUNTY MEDICAL SOCIETY MEETING; "Complications of Diabetes: Their Mechanisms and Management"; Doctors Cecil J. Watson, B. J. Kennedy, and Frederick Goetz, Department of Medicine, University of Minnesota; Auditorium of the North American Life and Casualty Company, 1750 Hennepin Avenue, Minneapolis; 7:30 p.m.

December 6-8  Continuation Course in Physical Medicine for Specialists

January 3-5  Continuation Course in Urology for General Physicians

January 7-9  Continuation Course in Dermatology for General Physicians

January 7  Hennepin County Medical Society Meeting

January 10  STUDENT AMERICAN MEDICAL ASSOCIATION LECTURE; Dr. Ancel Keys; Professor and Director, Laboratory of Physiological Hygiene, University of Minnesota.

January 15  MINNESOTA PATHOLOGICAL SOCIETY LECTURE; "Antibiotics Twenty Years After"; Dr. Wesley W. Spink, Professor, Department of Medicine, University of Minnesota Medical School; Owre Amphitheater; 8:00 p.m.

Jan. 31—Feb. 2  Continuation Course in Emergency Surgery for General Physicians

February 7-9  Continuation Course in Cardiovascular Diseases for General Physicians

February 7  GEORGE E. FAHR LECTURE; Mayo Memorial Auditorium; 8:00 p.m.
WEEKLY CONFERENCES OF GENERAL INTEREST

Physicians Welcome

Monday,  9:00 to 10:50 A.M.  OBSTETRICS AND GYNECOLOGY
         Old Nursery, Station 57
         University Hospitals

         12:30 to 1:30 P.M.  PHYSIOLOGY-
                     PHYSIOLOGICAL CHEMISTRY
                     214 Millard Hall

         4:00 to 6:00 P.M.  ANESTHESIOLOGY
                     Classroom 100
                     Mayo Memorial

Tuesday,  12:30 to 1:20 P.M.  PATHOLOGY
                104 Jackson Hall

Wednesday,  7:45 to 9:00 A.M.  PEDIATRICS
            McQuarrie Pediatric Library,
            1450 Mayo Memorial

Friday,  8:00 to 10:00 A.M.  NEUROLOGY
      Station 50, University Hospitals

         9:00 to 10:00 A.M.  MEDICINE
                     Todd Amphitheater,
                     University Hospitals

         1:30 to 2:30 P.M.  DERMATOLOGY
                     Eustis Amphitheater,
                     University Hospitals

Saturday,  7:45 to 9:00 A.M.  ORTHOPEDICS
            Powell Hall Amphitheater

         9:15 to 11:30 A.M.  SURGERY
                     Todd Amphitheater,
                     University Hospitals

For detailed information concerning all conferences, seminars and ward rounds at University Hospitals, Ancker Hospital, Minneapolis General Hospital and the Minneapolis Veterans Administration Hospital, write to the Editor of the BULLETIN, 1342 Mayo Memorial, University of Minnesota, Minneapolis 14.