1939

# Diabetic gangrene of the lower extremities

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# DIABETIC GANGRENE OF THE LOWER EXTREMITIES

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SENIOR THESIS

Senior Thesis presented
to College of Medicine
University of Nebraska
Omaha 1939

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# DIABETIC GANGRENE

## Introduction

Diabetes mellitus is a constitutional disease, characterized by glycosuria and hyperglycemia, which generally result from subnormal insulin production by the islands of Langerhans in the pancreas and as a result, a diminution of the ability of the body to utilize glucose. In addition there is a disturbance of lipoid and protein metabolism.

Diabetic gangrene is death or necrosis of tissue or an organ, partial or complete, in a person afflicted with diabetes, and having a pathology peculiar to itself, which entitles it to be classed as a definite clinical entity.

This condition was first reported by Marshal in 1852, in a report to the Academy of Medicine in Paris, in which he showed relationship between glycosuria and gangrene. However previously in 1806, Garco had pointed out that diabetics often suffered from ulceration.

## Importance of Condition

It is estimated by the Metropolitan Life Insurance Company that there are about 400,000-500,000 diabetics in the United States. One out of every ten diabetics develop gangrene, which necessitates surgical amputation.(19)

From 1930 to 1933, of diabetics admitted to Philadelphia

General Hospital, 175 or 13% developed gangrene, requiring surgery.(12)

Vogel reports his observation of cases of arteriosclerotic gangrene and diabetic gangrene during the period of 1912 to 1931 at the Surgical Clinic of the University of Leipzig. Of his cases, 197 cases suffered from arteriosclerotic gangrene and 117 from diabetic gangrene.(54)

Eliason remarks that the specter of gangrene is ever increasing with the prolongation of the life of the diabetic.(12)

Every untreated diabetic patient develops arteriosclerosis, and the causitive factors concerned are of great interest.

Joslin states: "Diabetic gangrene has been increasing as a menance to my patients. The percentage of mortality has risen from 2.3% prior to 1914 to 5.1% between that year and 1922 to 12.6%, from then until 1926 and since that year has decreased slightly to 10.4%." These represent deaths among patients seen by Joslin both in and outside the hospital since 1898.(19)

The mortality from diabetic coma as contrasted with gangrene has fallen in round numbers from 60% to 5%. Gangrene deserves more intensive study and the investigation of the cause and type of arteriosclerosis, which is responsible for it should help to defer old age for us all.

Carbohydrate Metabolism

In the normal animal, carbohydrate is used as fuel material in preference to protein and fat, and there is strong evidence to show that protein and fat must be converted to carbohydrate, before it can be utilized as fuel. It is not used as protein and fats in the process of tissue construction and repair, although exception to this statement must be made in that carbohydrates are used to some extent in this respect, as conjugated proteins and as fat compounds, as well as some being converted to regular body fat.

Carbohydrate is stored in a limited amount as animal starch or glycogen. When the amount of carbohydrate, which the body can assimulate is exceded, glycosuria results. The ability of the organism to utilize glucose depends on the rate at which the tissues are able to abstract it from the blood, the ability to oxidize it, the ability to polymerize it into glycogen or the ability to reduce it into fat.

Most of the sugar in mammalian blood is glucose and practically all of it is present in simple solution. The glucose is found to be fairly evenly distributed between the corpuscles and the plasma. The percentage of blood sugar is remarkable constant, not only in the same

individual but in different individuals, if no glucose is ingested.(6,11,28,51,53)

The storage of sugar is brought about by its conversion into glycogen and to a less extent by the raising of the sugar content of the blood and the extra-cellular tissue fluids. Sugar may accumulate in the skin and connective tissue.

The histo-chemical evidence of faulty carbohydrate metabolism is found in the absence of glycogen in structures, where depositon is a physiological function and the presence of glycogen in the tissues ordinarily free from glycogen.(2,11,49) Depletion of glycogen normally stored in the skin, liver and muscles is characteristic of preinsulin treated or uncontrolled diabetes. The change in the liver is one of abnormal storage, rather than depletion. Normally the glycogen is intra-cytoplasmic; in uncontrolled diabetes, it is intra-nucleic. Faulty deposition of glycogen in tissues normally free from it occurs in the kidneys. In uncontrolled diabetes, glycogen is found commonly in Henle's loop and convoluted tubules. Greater deposits of glycogen are found in the heart in untreated case of diabetes than in treated cases. Glycogen varies in amount in the smooth muscle of blood vessels, apparently, independent of the control of the disease.(53)

In a diabetic, the normal carbohydrate metabolism is

interfered with, and tissues are improperly nourished and, as a result may become pathologic and are more prone to succumb to deleterious processes.

The possible effect of fluctuations in blood sugar concentration in producing swelling of the intima, is considered as one of the predisposing factors in atherosclerosis.(2)

The concentration of the sugar in the connective tissue is not far from that in the blood and the arterial wall should be no exception to the rule.

These factors will be futher discussed under arteriosclerosis.

Lipoid and Cholesterol Metabolism

In a consideration of the atherosclerotic process which occurs in diabetics, one must bear in mind the disturbance of cholesterol and lipoid metabolism.

Normally the blood contains a considerable amount of fats and lipoids, varying somewhat, but not greatly, with the diet or with diseases. There is nearly a constant ratio between the fatty acids and the unsaponifiable lipoids (mostly cholesterol), and between the saturated and unsaturated fatty acids. Highly unsaturated acids are usually desaturated, preliminary to utilization. The proportion of cholesterol and lecithin is normally a constant, and these two lipoids seem to be functionally antagonistic, excess of either leading to pathological conditions.(38)

In various diseases, exclusive of diabetes, the total lipin content was found by Bloor to be about normal, but the proportion of the different lipin varied. In the study of diabetic blood, there has usually been noted a marked increase in the lipoid content and particularly cholesterol. This is more marked with acidosis. In general the lipoid percentage is increased with the severity of the disease and decreased when the disease is under control. (5,27,28) The lipemia is considered to be due to the inability of the body to adequately metabolize fat and thus the lipemia is increased or decreased according to the

fat intake of the diet.(12,32,35,36,)

Normal blood contains 0.16 to 0.17 per cent of cholesterol, of which about 55% is in the corpuscles. In pathological conditions, the cholesterol amount in the plasma varies greatly. Myxedema, nephritis and diabetes are the three conditions which are so often marked by high cholesterol values. In diabetes, there is a close relationship between high blood fat and acidosis.

It has been sugested that atherosclerosis may in part be due to method of diet.(24). That is: all of the cholesterol supply is ingested. It has not been proved that cholesterol is manufactured in the human body, at least in any great amount. Our diets do not fit in with the principle rules of food supply. That is, egg yolk is essentially for the embryo and milk is for the growing animal. The high cholesterol content of the pregnant woman denotes the mobilization of cholesterol for the fetus. Man is the only creature which routinely utilizes eggs and milk throughout life. Likewise man is the only animal to suffer from early atherosclerosis and to be universally afflicted with senile arteriosclerosis.

So in the diabetic various factors come into play. There is an essential defect in the ability of the body to mobilize and utilize lipoids. There is also the problem as to whether our present diets are unphysiological

enough to produce a tendency toward hyperlipemia and sequential pathological effects.

Insulin is a great advantage in regulating the cholesterol content of the blood. The age of the patient or the duration of the diabetes does not seem to influence the lipoid metabolism. Cholesterol value is considered by some to be a more important guide to the true condition of the patient than blood sugar.(40)

Clarkson points out the relationship between the ingestion of cholesterol and the production of atherosclerosis in the rabbit.(36)

Joslin does not entirely disagree with Clarkson's experimental evidence although Moschowitch points out that the lesions differed from true arterioscerosis as found in humans and that the same work was not able to be reproduced in carnivora.

Protein Metabolism

Protein metabolism in a diabetic, per se, does not show the marked changes or disturbance, seen with fat and carbohydrate metabolism. There is a normal minimal and perhaps a maximum intake of protein, which is desirable. This may be considered from ¾ to 1¼ grams per kilogram. In a diabetic the amount of protein necessary to carry on normal metabolism is desirable.

It is found that besides being the ultimate source of all body heat, food is a direct stimulant of heat production. This is known as the specific dynamic action of food. The specific dynamic action of protein is markedly higher than that of fats and carbohydrates. Thus protein liberates much free heat during its assimilation in the animal body and burns with a hotter flame than fats or carbohydrates. Protein stimulates the metabolism more than any other kind of food and favors the development of acidosis.

Excessive amount of protein metabolites have been considered to produce arteriosclerosis, but experimental evidence does not support this view.

It has been stated that there is a disturbed lipoid, carbohydrate, and protein metabolism in diabetes. This altered metabolism increases the tendency toward atherosclerosis in the diabetic.

In order to produce sclerosis of the vessels, it is necessary to have an abnormal intima. It is highly possible that in diabetes, fluctuations in blood sugar concentration produces a swelling of intimal ground substance, through changes in osmotic pressure.(24)

Biopsies of skin from a number of diabetics have been examined histiologically for glycogen content. In those with high blood sugar, the connective tissue of the corium was slightly edematous and staining basophilic, strongly resembling the change seen in the intimal ground substance of early arteriosclerosis.(27)

Virchow first accurately described this process as a loosening of connective tissue ground substance, of which the arterial intima is largely concerned. There is a swellin of ground substance due to an increased imbibition of fluid elements. This may be recognized microscopically by increased width and homogenicity of connective tissue spaces.

Adami and Winaus considered that the atheromatous fatty process, depended solely in the deposit of cholesterol esters.

Hypertension is not prominent in arteriosclerosis of the diabetic type, and in view of the increased prevalence of arteriosclerosis in diabetics, it probably plays a factor in relatively few cases.

In the University Hospital, only 5 of 31 cases showed increased blood pressure. The majority of cases showed normal or even relatively low pressure. This would indicate that hypertension plays little part in the development of arteriosclerosis, although it may be a coexisting condition.

Kramer found that in a study of 500 cases of diabetes, there was a systolic pressure of 150 mm. or above in 39% of cases.(55) His figures are higher than those of other clinics.

Infection does not play a direct factor in the production of arteriosclerosis in a diabetic. However toxemias of infections and acidosis may play an important part in damaging the vessel walls.

Thus according to Aschoff and Virschow, given an abnormal intima, a high blood lipid content will tend to produce arteriosclerosis. This has resulted in our present concept of low fat diets in the treatment of diabetes.

Arteriosclerosis

In the non-diabetic, the vascular pathological changes that are encountered are fairly closely correlated with the different types of vessels. The atheromatous plaque is the characteristic arteriosclerotic lesion of the elastic arteries. This may present several forms, all of which are probably related and represent various stages in the process of atheromatous degeneration.(49)

According to Aschoff, the first stage is the so-called atheromatosis of puberty, characterized by fine yellowish sub-endothelial streaks, particularly about the orifices of the intercostal arteries. These areas are translucent and slightly raised and the vessel maintains its normal elasticity. Microscopically, there is a swelling and loosening of the intercellular substance of the intima, chiefly in the deeper layers, with deposition of minute fat droplets. The fatty infiltration is far more marked in the intercellular substance, than in the cells themselves. As the process develops, more and more of the intima is involved until finally the endothelium is reached.

"The next stage in the development of true arteriosclerosis is fundamentally the same. There is however, a more marked swelling and hyaline change of the ground substance of the intima with infiltration of lipoid and new formation of fibrous tissue, which in turn becomes hyalinized. Beneath the hyaline connective tissue, there may or may not be an enormous mass of atheromatous material. Finally,

necrosis of the tissue cells, occurs with decomposition of the cholesterol esters to the characteristic needle-shaped cholesterol crystals and fatty acids, which sooner or later combine with calcium. These calcium soaps become the calcareous or even bony plaques formed in the atheromatous regions. As the plaque becomes larger and reaches nearer the surface, the blood stream may sweep away portions of the putaceous material, forming the atheromatous ulcer. Aschoff emphasizes that the lipoid content of the plasma does not cause the atheromatosis, but influences the character of the atheromatous plaques by determining the degree of fatty infiltration of the hyalinized ground substance.

The second type of arterial change is that seen in the muscular vessels. Here medial calcification predominates. This lesion is entirely distinct from the atheromatous process which is seen in elastic vessels and is found only in the muscular vessels. In this type intimal change is negligible and the lumen remains intact or is even actually widened. The initial change is the deposit of granules of calcium in the connective tissue stroma about the muscle cells. This calcification gradually becomes more and more abundant, finally surrounding and causing atrophy of the smooth muscle cells. There is little relationship between the occurrence of this type of arteriosclerosis and the atheromatosis, although they may coexist.

The third type of arterial disease is that known as thrombo-angiitis obliterans or Buerger's disease. This type usually occurs in young adults. Here the physiological, pathological process consists of thrombosis, organisation of the thrombus and subsequent partial recanalization of the thrombosed vessels. Calcification is absent as is the deposition of lipoids.

A fourth type of vascular change is met with in the smaller arteries and arterioles. This is called obliterative endarteritis. The pathology consists of a hyalin thickening of the intima.

In the diabetic patient, the atheromatous type of lesion is the outstanding one. One thing which is indicatory of diabetic sclerosis is the intimal type of involvement in the muscular arteries, either alone or superimposed upon the medial calcification.

"Atheromatosis i.e. lipoid deposition into the intimal structure, and atherosclerosis( atheromatosis, complicated by connective tissue overgrowth), from a clinical point of view appear to be similar in the diabetic and the non-diabetic aortae, but there is a greater deposit of lipid, a more marked change in the lipid allocation, and a higher calcium and phosphorus content in the diabetic aortae"(27)

The chemical difference in the two processes appears to be in the exageration of the process in the diabetic.

In order to explain the increased calcification occurring in the diabetic, it is necessary to consider the conditions which are peculiar in the diabetic patient. Hyperglycemia, lipoidemia, ketonemia and diminished carbon dioxide content of the plasma during periods of acidosis have been regarded as etiological factors.

A high plasma lipin content forms a good medium from which lipid deposit may occur and pathological observations, indicate that lesions in the intima are in part due to its deposition.(2,49)

The high plasma lipid content of the diabetic patients, should make the formation of atheromatous lesions, easier provided the etiological agents for initiating physicechemical changes in the intima, which predispose to lipid deposition are present too. That hypercholesteremia is not the only factor in atherosclerosis is indicated by the repeated failure to reproduce that lesion in carnivora with diets rich in cholesterol.(16,17)

McNealy says: "We know that as the diabetic factor becomes more and more prominent, intimal changes in the muscular arteries become more and more prominent in comparison with medial changes. Fat deposition in the internal elastic becomes more and more prominent and medial calcification falls behind in the arteriosclerotic process." (56)

The severity of the disease, when adequately treated with diet and insulin appears to have little influence upon the blood cholesterol, possibly because the majority of the patients are mild diabetics. The following chart illustrates this point.(16)

| Severity | Cases | Age | Duration yrs. | Chol. mg% | Blood S. % | Insulin U |
|---|---|---|---|---|---|---|
| Mild | 196 | 45 | 7.4 | 224 | 0.19 | 12 |
| Moderate | 24 | 20.8 | 7.0 | 207 | 0.20 | 33 |
| Severe | 50 | 28.1 | 6.0 | 256 | 0.26 | 45 |

"Whether the increased prevalence of arteriosclerosis in diabetes is due to the disease itself or to methods of treatment of the disease, the importance of the problem is such that it cannot be disregarded."(49)

Warren states that formerly every case of diabetes with a duration of five years had arteriosclerosis, regardless of age. However in recent years he reports 4 cases autopsied without arteriosclerosis. That the heart and bloodvessels were affected in the preinsulin group of young diabetic patients is shown by 3 of the 4 preinsulin cases reported by Naunyn, who found evidence of atheromatosis when the duration of the disease varied from five months to three years, and the 6 of the juvenile

cases, studied by Dr. Shields Warren. They had atheromatous lesions, which were evident from the first week to the twenty-ninth year. These changes occurred in only slight degree in the one case, whose disease had been treated for an appreciable time with insulin.(53)

It has been shown that diabetics are afflicted with arteriosclerosis, which is similiar in character to arteriosclerosis in a non-diabetic, but varies as to degree and involvement.

One might ask as to what clinical bearing, the character of arteriosclerosis has in regard to the type of gangrene.

Gangrene in a diabetic patient may be divided into:

1. Senile or arteriosclerotic
2. Embolic
3. Gas gangrene
4. True diabetic gangrene.

Senile gangrene shows a pathological calcification of the media, with fibrous thickening of the intima. This is due to the gradual occlusion of the larger vessels, usually with superimposed attacks of thrombosis, the process of occlusion being more rapid than the establishment of collateral circulation, with resultant atrophy and gradual mummification of the part. This type of gangrene in a diabetic is similiar to that of a non-diabetic. Clinically the diabetes is usually mild. Extensive general arteriosclerosis is present. Frequently a past history of attacks of pain or numbness, or tingling of the foot is obtained, indicating the thrombosis of one or more of the arteries.

Embolic gangrene has a sudden onset, usually with severe pain or a sensation of burning caused by the sudden occlusion of a large vessel, due either to an embolus from some distant source (often the heart) or to the sudden development of an occluding thrombus on the wall of a vessel as a result of acute infection, such as pneumonia. Gangrene usually develops rapidly, its distribution depending largely on the vessel occluded. The prognosis is

usually bad because of the primary pathology. This type is no more common in the diabetic than in the non-diabetic.

Gas gangrene can be associated with other gangrene or it may be the primary factor.

True Diabetic Gangrene has one striking difference from arteriosclerotic gangrene in that diabetic gangrene is a wet gangrene. Arterial occlusion in the typical diabetic gangrene is a gradual process, a progressive encroachment on the lumen of the artery by intimal thickening, not infrequently, showing heavy deposits of lipoid. There is usually time for collateral circulation to develop. While there may have been pain and disability during the process of readjustment, eventually a delicate point of equilibrium is reached where the combined supply of main vessels and collaterals is just sufficient for the ordinary needs of the limb. Any abnormal condition finds that there will be insufficient blood supply to maintain tissue life and yet too good a supply to permit mumification. Moist gangrene is the result. Thus diabetic gangrene is a clinical and pathological lesion, which is a definite entity. The literature and hospital records do not sufficiently make a separation between diabetic gangrene and senile gangrene in a diabetic person.

Etiology

"The vascular condition is the underlying and determining factor in the cause of diabetic gangrene."(12) However there is usually associated a "trigger insult", which is the primary cause of the gangrene. In other words tissues laboring under disturbance of their fat and carbohydrate metabolism and suffering from a diminution of their vascular supply due to the pathology of the extremity vessels, are given an added insult which terminates in the failure of metabolism and tissue nourishment to be adequately sustained and gangrene results.

The most common insult is trauma and infection. However any added load to overburdened extremity vessels is a factor in the production of gangrene. The insult is quite often a blister, a corn, a bruise, and is often followed by or accompanied with infection.

Joslin states that the most important factors in prevention is treatment of the diabetes, which is designed to prevent early disease of the arteries, and second upon cleanliness of the feet and third, upon those conditions which might predispose to an infection of the feet.

Speaking of foot hygiene, Joslin states: "This is the reason for our Beauty Parlor for Diabetic's Feet at the Deaconess Hospital. In the first place injuries to the feet should not occur. --- Warning and admonition should

penetrate so deeply the minds of your cases that if such a catastrophe should ever occur, the unhappy patient will feel compelled to say: "Doctor, you warned me about injury to my feet, about the dangers in cutting corns, toe nails, about blisters from new shoes or old shoes with poor linings, about nails in my shoes, flat-foot plates and hot-water bags. You are not to blame for my present condition."(22)

"Trauma is notorious as the cause of many cases of diabetic gangrene. Here again prevention is the important feature. Every known patient with diabetes, should be warned, threatened, or even frightened in regard to the danger of home surgery, such as cutting corns, calluses, or ingrown nails.--- The physician should not consider it beneath his dignity to properly perform this minor procedure for any patient with diabetes."(41)

The hygiene of the feet is most important. A most frequent point of origin of diabetic gangrene is a fissure in an interdigital space. This fissure is almost always caused by an infection of epidermophyton. Epidermophytosis or ring worm is quite common among individuals. Joslin found 40% of his diabetics had it. Hulsy found 67% of University students had it. For this reason the hygiene and prophylaxis of the diabetic foot must include serious consideration of ringworm infections of the interdigital spaces.(41,28, 22)

The danger lies not so much in the ringworm itself as in the introduction of secondary, pyogenic invaders into the fissures and open lesions caused by the primary organism. As soon as the secondary infection is established, the mischief is done--- local edema and infection soon cause small areas of superficial gangrene in the interdigital spaces. The pressure of the edema in the poorly nourished tissues causes further extension of the gangrene, usually toward the base of the adjacent toes. Thus the existing diminished blood supply to the digits is shut off completely and within a short time discoloration and gangrene are observed.

At the first sign of impending gangrene, complete rest is imperative, not only because of the removal of local trauma but because of the necessity of maintenance of the limb in the horizontal position for even a short period of time, lessens the edema of the foot, and particularly of the involved area.(41,30)

Another point of origin of gangrene is a small fissure on the heel. Prevention of this condition is usually simple, if the possibility of its development in all cases of deficient circulation is kept in mind. Diabetic gangrene of the heel, may also develop from constant pressure on the bedding while the patient is being treated for some other condition.

Climate

Beard of Minneapolis reports 95% of his gangrene cases occurred during the winter months.(55)

Blotner and Fitz in reporting 69 cases of diabetic gangrene at Peter Brent Bringham Hospital in Boston observed that their cases also showed a greater frequency in the colder months of the year than during the warmer months, although their experience was not as striking as Beard.(57)

Paullin reports few cases seen in Georgia. Lehman in studying the influence of climate showed these figures:

| Clinic | Adm. | Cases | Gangrene | % |
|---|---|---|---|---|
| Joslin | | 3000 | --- | 3 |
| Paullin (Georgia) | | 560 | 15 | 2.55 |
| Mass. G.H. | 33,734 | 600 | 55 | 9 |
| Peter Bent B. | | 969 | 69 | 7 |
| Boston C.H. | 148,621 | 439 | 79 | 18 |
| Touro Infirmary | | 201 | 20 | 10 |

He found that the per-centage in the whites was 14% and in the negroe 21%. He concludes that the increased incidence was due to the poorer hygiene of the negroe. Joslin

points out the experience of Muryama and Sakaguchi, who did not have a single death from gangrene in their 49 cases of diabetes and this despite the marked arteriosclerosis of Japanese diabetic patients. He points out that the Japanese wear soles, which do not compress their feet and are scrupulous in the hygiene of the feet. The high incidence in winter months reported by some, may be due to the greater increase in trauma in the winter, either direct freezing or injury.

Obesity prior to the onset of diabetes is present in a large percentage of patients who develop gangrene. Root found that the average weight of 22 cases of gangrene in his series to be 210 pounds.(40)

Age is a determining factor and the average case of gangrene is over 60 years of age. In the University of Nebraska Hospital, the youngest case was 44 and the oldest 74, with the average between 60 and 70. McKittrick reports that the average age of 74 patients with diabetic gangrene was 64.11 years. There are relatively few cases between the ages of 40 and 50.(22,30)

Syphilis used to be considered an etiological predisposing factor in diabetic gangrene. The number of positive serology cases, varies from 1% to 3% with various clinics. (22,25)

In considering the etiology of diabetic gangrene one must consider that there is a deficient blood supply to the area, there is a deficient tissue nourishment, due

partly to the deficient blood supply and partly due to the faulty tissue metabolism caused by diabetes. Given such a background one can see that any added load might tip the balance and gangrene result.

Diagnosis

Peculiarly diabetic gangrene usually has no significant prodromal local symptoms, prior to the onset. Many individuals do not know they have diabetes until they present themselves to the physician for treatment of a necrotic area of the extremity. So important is this factor, that routine urine sugar examinations, should be made on any suspicious extremity lesion.

In a patient, who is not of the complaining type, or in those who are poor observors, symptoms of diabetes may be passed over and entirely missed. Thus the importance of good histories of patients must be taken, as this often offers a lead to the trouble. Thus every patient in whom diabetic gangrene is suspected, a careful clinical history should be obtained, for occasionally a urine analysis may show no sugar in the particular sample examined. This is not the usual experience, but occasionally if routine sugars on each sample in twenty-four hours are run on some patients with diabetes, there will be some samples which show little or no sugar. This is more true of the early morning sample. However careful history may reveal history of polyuria, polydypsia, polyphagia, pruritis, and loss of weight. Any one of these factors should lead the clinician to suspect diabetes. A fasting blood sugar and a glucose tolerance curve will establish the presence or

absence of diabetes in doubtful cases.

As in other conditions in medicine, presented with a case of gangrene in a diabetic, the physician should classify the disease. The most frequently encountered are dry (senile) gangrene or true diabetic (wet) gangrene. The dry gangrene may be complicated by infection and may become a wet gangrene.

The true diabetic gangrene is either infected or should always be considered potentially infected. The management will depend upon the condition found.

Dry gangrene is usually always caused by a thrombosis of one or more of the important arteries, usually preceded by a gradual narrowing of the lumen of the vessel by arteriosclerotic process. The gradual development of this occluding process allows the collateral vessels to become fairly well opened before the extremity is forced to depend upon their blood supply. This process may be accompanied by discomfort or pain. If the occlusion has been more or less sudden or so high that blood supply is shut off at one time, gangrene of one or more toes will develop. It is in such a leg, that definite skin temperatures and color changes can be demonstrated.

In true diabetic gangrene, the person has outlived the period of reorganization, without any great difficulty or catastrophe. The foot has a collateral circulation

and a narrow margin of safety. With no precipitating factor, the extremity will have no difficulty. However a minor injury causes infection and thrombosis of the small but important vessels and gangrene is the result.

Local tissue metabolism being "under par and vascular supply being diminished, the body is unable to localize the process and lymphangitis and tissue infection are the result. This is true diabetic gangrene. In the literature, in hospital records, and in clinical discussions, this difference is not made clear and as a result statistics in most clinics do not suffieiently distinguish between senile gangren in diabetics and true diabetic gangrene.

The recognition of diabetic gangrene is of great importance, because it is in this group where prevention can show results.

Recognition of the extent of collateral circulation, will help in the conservative treatment of early gangrene. Thus with senile gangene in diabetics, with lack of pulsation of extremity vessels, the surgeon would have to amputate higher than with adequate collateral circulation.

In all cases of gangrene, careful study of the extremity must be made before treatment is undertaken.

Circulation

In all cases the condition of the peripheral arteries must be determined. There are many laboratory tests to determine the adequacy of circulation. Because of the added expense, technical difficulties and errors, they

do not offer as much as clinical examination and judgment.

"For comparison, both limbs should be tested. The femoral, popliteal, posterior tibial and dorsalis pedis should be routinely examined. Of these, the dorsalis pedis is the most important clinically, being palpable in practically every normal individual. The posterior tibial is more difficult to palpate and less important clinically. Although good pulsation of the dorsalis pedis and posterior tibial arteries is a favorable sign, it does not preclude gangrene of a toe due to an occlusion of a digital vessel." (14)

The findings must be evaluated and an absence of pulsation does not mean that gangrene is impending or that a lesion already present will spread, since an adequate collateral circulation may be present.

The dorsalis pedis artery lies just lateral to the extensor hallucis longus tendon, and is best palpated between the proximal ends of the first and second metatarsals. It is sometimes variable in its course and sometimes difficult to feel. The character of pulsation varies from day to day and may be felt easily on one day and with difficulty the next. Sometimes the twitching of the tendon or the pulsation of the artery in the fingers of the examiner may interfere with the test. McKittrick recommends that the right dorsalis pedis

artery be palpated with the flexor surface of the tips of the second, third, and fourth right fingers, the thumb of the examining hand being on the sole of the foot, where it readily steadies and directs the amount of pressure to be exerted. The examiner then finds his own radial pulse with the thumb of his left hand. When pulsations are felt which are taken to be those of the dorsalis pedis, gentle pressure on the examiner's radial artery with his left thumb will stop sufficient circulation to the examining fingers, so that any pulsation felt subsequently will be from the patient.

The posterior tibial artery is located by allowing the tips of the fingers to rest on the hollow behind or below the internal malleolus. If present, pulsations can usually be felt, except in the presence of edema.

The popliteal artery is at times difficult to feel, particularly in a large leg. It generally lies on the outer side of the mid-line in the popliteal space, and is best felt by standing on the side to be examined, placing the thumb of the examining hand in the niche just above or below the patella and palpating with the flexor surfaces of the third and fourth fingers. Pressure can be varied easily and the vessel usually found between the mid-popliteal region and the external hamstrings. Another method advocated by Buerger is to have the patient lie face down, the leg flexed at the

knee to a right angle and held in the desired position with one hand of the examiner while, with the fingers of the other hand, the popliteal region is easily palpated.

COLOR CHANGES

Much can be learned from the color of the extremity. A dusky, cyanotic extremity indicates poor circulation. The color change is very important and especially the color change should be noted with change in position. If the extremity shows pallor upon elevation and duskiness when lowered, it indicates very poor circulation. This color change indicates the extent of good collateral circulation and where the color demarcation becomes evident, marks the beginning of inadequate circulation. Both legs should be compared for color change. The color change may involve only the tips of the toes or extend up to the mid calf, depending on the level at which the larger vessels are occluded, the degree of occlusion and the amount of collateral circulation developed. (13,14,32,46)

SKIN TEMPERATURES

Skin temperature variation goes hand in hand with color change in the study of gangrene. It is a simple procedure, requiring only a brief time to determine. In this procedure, the hand is run lightly over the extremity from thigh to toe and drop in temperature noted. Usually with inadequate circulation there is a marked drop

which corresponds fairly well with the color demarcation. Both extremities should be compared. Both the color change and the skin temperature will be more evident with the patient sitting up and both feet dependent, than with the patient lying in bed. Of course, in many normal individuals, the feet are usually colder than the thigh, but the object of this test is to determine a marked change or relative sudden change in temperature and especially a variation with the opposite extremity.

NUTRITION

With deficient blood supply, there is usually disturbance of nutrition. This may sometimes be evidenced clinically by a waxy appearance of the skin, loss of subcutaneous fat and at times, an extensive atrophy of the foot and calf muscles. This malnutrition may or may not be marked but should always be observed.

BLOOD PRESSURE

Blood pressure does not give any indication as to the degree of sclerosis. In 31 cases of diabetic gangrene in the University Hospital, only four showed diastolic pressure of a hundred.(page 24) On the other hand many cases showed a markedly low systolic and diastolic pressure. Rosenbloom states that in every case of diabetic gangrene in which the blood pressure is high, there is a complicating disease. Of course the fact that an individual has diabetes is no reason why

hypertension can not exist in the same individual. But the blood pressure gives no indication of the sclerosis due to diabetes, at least in the early stages, as in these cases of gangrene mentioned, Xray showed a more or less marked calcification of all extremity arteries.

XRAY

Xray of the extremities in gangrene is not of great value except in the presence of infection, in which case it provides a valuable means to determine the presence or absence of bone involvement. Almost every case of diabetes above 40 and many as early as the age 16 show arteriosclerosis by Xray. Thus Xray does not offer much aid because one may have good physiological circulation and adequate circulation by clinical tests, and yet by Xray, the extremity may show a marked degree of sclerosis. Visualization of the arteries by injection of opaque substances into the main artery,followed by Xray examination is a procedure which should be condemned. It is accompanied by too much danger and offers nothing which simpler tests will not show.

ARTERIAL SPASM TEST

The amount of dilatation of the arteries may be determined physiologically by the simple procedure of immersing the extremity in warm water (110-115) and comparing the temperature after 20 minutes with the skin temperature before immersion. A skin thermometer or a

thermocouple can be used for this purpose. Another test along this order and in some ways more simple is the histamine test.

HISTAMINE TEST

This test is based upon the observation of Lewis that interruption of the circulation in an extremity prevents the normal development of the skin reaction to histamine. The test is carried out in the following manner. The skin area to be tested is cleansed with alcohol which is allowed to evaporate to dryness. A drop of 1:1000 aqueous solution of histamine acid phosphate (15% chloretone is added as a preservative) is placed on the cleansed area, and the skin is pricked seven times through the drop, the pricks forming a circle about 5 mm. in diameter. The reaction consists of a wheal surrounded by a reddened area which in individuals with normal circulation appears within five minutes. The greater the degree of circulatory failure, the longer the time before this reaction makes its appearance. The patients must be placed flat upon their backs with the legs extended during the test. The areas chosen for the test were just above the knee, the upper and lower thirds of the leg, and the dorsum of the foot. The cases are graded according to the time of appearance of the reaction and it was found that the intensity of the reaction was inversely proportional to the time

factor. Grade 1 or normal reaction was complete within five minutes. Grade 2 was complete within ten minutes. Grade 3 were considered to be those with incomplete reaction after ten minutes, having a normal control above the knee. In one group of 100 unselected diabetics under treatment, the response of the skin to the histamine test indicated that 32% had normal circulation. In 34% the circulation was somewhat impaired and 34% had marked impairment of circulation.

In a study of the clinical course of 89 patients tested 5 years previously, no Grade 1 reaction had any serious trouble with the feet during the intervening period. Grade 2 likewise had no trouble of a serious nature, although pain was reported by 4 of them. In the Grade 3 group, the situation was quite different. Only 14 of the original 34 survived the 5 year period and only 5 of these survivors had avoided serious trouble with their feet.

The information from the histamine reaction must be supplemented by consideration of the physical findings, the age and other clinical information.(44,45)

Treatment

Whether the problem is diabetic gangrene or senile gangrene, the treatment will depend on the vascular condition of the extremities. The treatment of diabetic gangrene is divided into the medical and surgical. Its treatment is an illustration of the close cooperation which must exist between the physician and the surgeon and whether these two parts are played by the same man or delegated to a physician and surgeon, the factors underlying treatment are always present. That is, diabetic gangrene is always a medical problem. As mentioned previously diabetic gangrene is localized pathology in a general disease. Sometimes the surgical angle becomes the primary emergency and must be treated as such.

At the first sign of impending gangrene, complete rest is imperative, not only because of the removal of local trauma but because of the necessity of maintenance of the limb in the horizontal position. If the extremity is held in the dependent position for even a short period of time, edema of the foot, and particularly of the involved area, soon appears. This causes greater pain and extension of the gangrenous process. Elevation of the foot is harmful, since it causes further depletion of the blood by the force of gravity.

The object of the local treatment of gangrene in the

diabetic is to prevent, as far as possible, the spread of infection in the gangrenous area with its ultimate extension. Dry heat should always be used instead of any form of wet heat, but there is danger in increasing metabolism above the level where a deficient circulation is capable of providing sufficient tissue nutrions.(11) Control of the diabetes is of course most important because it has been shown that tissue metabolism is under a strain in diabetes. The conservative management should not be carried so far that the general well being of the patient is endangered. Sometimes it is necessary to surgically intervene in order to bring the diabetes under control.(1,15,) Surical intervention in gangrene is a matter of clinical judgment. This paper will not deal with the various procedures and methods of operation. The extent of amputation will depend upon the extent of adequate vascular supply. The time of operation likewise varies with each individual case. In general the less trauma at operation, the better the end results. In considering surgery, one is confonted with the two problems of saving the patient's life and of making that life a useful one.(4,12,13,14,17,52)

Prognosis

The prognosis, even with operation, for severe gangrene is uncertain and the final mortality is high, about 17%.(30) This mortality can be reduced by earlier treatment, but there are many factors which must be borne in mind. Perhaps the greatest factor is the age limit, actual and relative. The average age of diabetic gangrene is about 64. Also it must be remembered that the vessels and body tissue in a diabetic are at least 10 years older than if the patient did not have diabetes.

Thus one is combatting a generalized disease with sclerosis of all vessels and particularly the heart. Then, the period of rest in bed is long, and many succumb to pneumonia, which causes the exit of so many of the aged. However, as in cancer one recommends early treatment, so if in diabetes, the treatment is earlier, the prognosis will be better. The immediate results from surgery of gangrene are usually good but the ultimate prognosis is bad. The most hope still lies in prophylaxis, which will be discussed.(14,19,33,)

Prophylaxis

True diabetic gangrene is largely preventable if sufficient care is given to the extremity. That is, diabetic gangrene had already shown an ability to readjust itself to the sclerosing process and it is the added insult, which causes the gangrene, producing the characteristic pathology.

The aim should be to prevent the development of arteriosclerosis. Perhaps controlled diabetics, with low fat diets, will lessen somewhat this tendency of arteriosclerosis. This must await future work.

However at present, the care of the extremities is the important part in prophylaxis. Every diabetic should preserve in the best possible manner as much of the vascular supply as he can. Buerger's excercises should be practiced routinely by the diabetic.

Circulatory aids

1. Excercise:

   The legs should be exercised by lying flat upon the bed, raising the foot to a verical position for one minute, then allowing them to hang over the side of the bed for one minute and then rest them on the bed for one minute and repeat this exercise five times, from one to three times daily as prescribed.

2. The patient should guard against excessive heat or cold, as excessive heat may burn and raises the metabolism; and cold decreases the circulation.

Care of Feet

Proper care of the feet must be taught to every diabetic. The diabetic should be on guard for any unusual condition:

Conditions requiring attention

1. Ring worm infection or Epidermophytosis
2. Dry, scaling, atrophic skin
3. Cold feet
4. Thick, dry, brittle nails
5. Cramps and stiffness
6. Discolorated areas
7. Clammy, moist skin
8. Trauma

All these conditions should be given the most careful consideration by the physician if gangrene is to be avoided. Every diabetic should practice routine foot hygiene and should do this religiously. It would be well for the physician to outline the care which should be given to the feet.

General hygiene:

1. Wash feet daily with soap and water. Dry thoroughly especially betwee toes.
2. When thoroughly dry, rub well with hydrous lanolin, as often as necessary to keep skin soft, and free from scales and dryness. If nails are brittle and

dry, soften by soaking in soft water one-half hour each night and applying lanolin generously under and about nails and bandage loosely. Clean nails with orange wood sticks.

3. Cut nails straight across and avoid injury to the toes.
4. Wear shoes which do not bind or rub.

Treatment of abrasions:

1. Proper first-aid treatment is of utmost importance.
2. Thorough cleanliness with soap and water.
3. Avoid strong, irritating antiseptics. Apply weak antiseptic.
4. Cover with lanolin on sterile gauze and light bandage.
5. Avoid using the foot as much as possible. Bed rest may be necessary with leg in horizontal position.

Treatment of corns and callosities.

1. Wear shoes which cause no pressure.
2. Soak foot in warm soapy water, dry and rub or file off dead skin. Then pain the corn with this mixture. (salicylic acid one drachm, collodion one ounce) Repeat for four nights then, after soaking in warm water, the corn will come off easily.
3. Do not cut corns or callosities.
4. Wear pad to distribute pressure if necessary.

# DIABETIC GANGRENE IN U of N HOSPITAL

## June 1933 - March 1939

| | Duration | Sex | Age | B.P | Treatment |
|---|---|---|---|---|---|
| 1. | 5 yrs. | M | 70 | 165/70 | Amp. of L. ft. |
| 2. | 7 yrs. | F | 46 | 112/65 | Amp. of L. toe |
| 3. | 3 yrs. | M | 66 | 152/86 | Gangrene, no operation |
| 4. | 12 yrs. | M | 74 | 130/60 | Amp. of toe |
| 5. | 6-7 yrs. | M | 48 | 98/66 | Amp. of toe |
| 6. | 7 yrs. | M | 66 | 150/85 | Amp. of toe |
| 7. | 6 wks. | M | 44 | 130/70 | Amputation |
| 8. | - | M | 44 | 130/70 | Amp. of R. Leg, gg, died |
| 9. | 13 yrs | M | 53 | 100/50 | Abcess drained |
| 10. | 6-7 yrs | M | 50 | 110/65 | Toe slough |
| 11. | - | M | 49 | 160/100 | Amp. of R. leg, and L.toe |
| 12. | 1 yr. | M | 57 | - | Amp. of L. leg |
| 13. | 10 yrs. | M | 62 | 130/72 | Amp. of R. ft. |
| 14. | 10 yrs. | F | 70 | 150/70 | Amp. of R. toe |
| 15. | 4 yrs. | M | 61 | 140/78 | Amp. of toe |
| 16. | 16 yrs. | M | 62 | - | Amp. R. leg |
| 17. | 18 yrs. | M | 60 | 160/100 | Amp. R. leg |
| 18. | 16 yrs. | M | 68 | 124/86 | Amp., died |
| 19. | 6 mo. | M | 53 | 156/70 | Amp. L. leg |
| 20. | 10 yrs. | - | 66 | 200/110 | Amp. L. toe |
| 21. | 1 yr. | M | 52 | 136/84 | gg., died |
| 22. | 5 yrs. | F | 69 | 150/90 | Amp. leg |
| 23. | 2 yrs. | F | 58 | 170/80 | Amp. of L. leg |
| 24. | 6-7 yrs. | M | 48 | 98/66 | Refused operation |
| 25. | - | M | 74 | 146/ | Amp. of toe |
| 26. | 6 yrs. | M | 48 | 98/66 | Amp. of toe |
| 27. | - | F | 55 | 147/72 | Amp. of L.leg., died |
| 28. | - | F | 74 | 130/60 | Died, no amputation |
| 29. | 1 yr. | M | 66 | - | Gangrene, no operation |
| 30. | 10 yrs. | M | 73 | 190/100 | No operation |
| 31. | 1 yr. | M | 61 | 145/90 | No operation |

## Conclusion

The diabetic patient presents an interesting problem to the clinician and to the research worker. Diabetics develop arteriosclerosis at an earlier age and to a much greater degree than does a non-diabetic. Whether this is due entirely to the altered metabolism or has been influenced largely by former methods of treatment must wait future evidence. The influence of diet and the factors which produce arteriosclerosis are problems which have not been sufficiently and adequately worked out.

Due to the sclerosis of the vessels and to the altered tissue metabolism, diabetics are confronted with the fact that the well being of their extremities have a narrow margin of safety.

Any insult, which places an added burden on the extremity, may upset the balance and diabetic gangrene result. This is a wet gangrene and has a characteristic clinical history and pathological findings. It differs from senile gangrene in that the extremity has already made a vascular adjustment and were it not for some precipitating factor, the condition would not result.

Diabetic gangrene can to a great degree, be prevented by the realization of the causative factors and by a careful regimen, which provides for scrupulous and adequate care of the extremities.

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