of serum iron, the iron-binding capacity of the serum proteins, the serum copper, and the protoporphyrin were investigated in normochromic anaemia and in hypochromic anaemia. In true iron-deficiency states these show a characteristic pattern which is quite different from the normal. This characteristic pattern was outlined in nine cases of microcytic hypochromic anaemia, and the regeneration towards normal was studied when these cases were given intravenous iron.

We are indebted to Professor James Young and Professor E. J. King for access to their patients and for the facilities to do this work. One of us (S.V.) is receiving a British Council grant. Mr. T. Simmonds kindly carried out all the haemoglobin determinations and cell counts.

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A note in the *New York Times Supplement*, November 4, describes some American experience with the new way of killing rats and mice with "warfarin." This contains dicoumarol, the blood anticoagulant often used in the treatment of thromboses, which was introduced for pest control by J. A. O'Connor in Malta in 1947. The anticoagulant is presented in the form of a food bait which is eaten fairly readily by animals over a period of time: internal bleeding occurs in 5 to 14 days, and they die from anaemia and shock, particularly if their normal blood volume is small, as is the case in rats and mice. The risk to pets is slight—a cat would have to eat several poisoned mice daily for at least a week to suffer ill-effects, while on farms the greatest danger is to hogs. There are estimated to be at least 300 million rats in the U.S.A., and one extremely successful rat-killing campaign in Texas is mentioned where 15 lb. of warfarin destroyed 550 rats. It is suggested that research should be carried out on other anticoagulants, which may prove more effective than dicoumarol in waging biological warfare on rodents.

DIABETIC GANGRENE

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There is still a tendency in many places to proceed at once to radical surgery in diabetic gangrene, mainly because it is felt that, as in senile gangrene, nothing less than amputation, usually of the above-knee type, will arrest the progress of the disease. It is our aim in this paper to show that conservative surgery has a very definite place in treatment, and that it will in most cases leave a useful limb with a minimum of disability.

Diabetic gangrene can be divided into two types: (1) those cases in which infection is the primary factor; and (2) those in which occlusive vascular disease is the exciting cause.

The former type is found among the younger patients and is much less common than senile diabetic gangrene. The arterial tree appears perfectly normal, and so are the pulsations throughout the limb. The gangrene is due to primary infection followed by secondary thrombosis of the digital vessels. Occasionally the condition is well advanced before the patient is seen, owing to the associated diabetic neuritis and its resultant hyposensitivity and loss of pain.

The treatment of these cases, no matter how advanced the gangrene may appear, is definitely conservative. If possible the sensitivity of the organisms should be determined in order to indicate the correct antibiotic and chemotherapeutic agents to be used, and x-ray examination is necessary to exclude the presence of suppurative arthritis or osteomyelitis of the phalanges and metatarsals. Surgical treatment is limited to complete excision of all gangrenous tissue and adequate drainage of the affected tissue planes.

These simple measures are usually effective and only in exceptional circumstances is amputation necessary. The diabetic condition demands very careful supervision owing to the profound disturbance of metabolic balance resulting from the infection, but we have found that stabilization takes place almost immediately the infection is controlled.

The latter type is that which occurs in elderly patients; in these, degenerative changes in the peripheral blood vessels lead to decreased vitality in the tissues and diminished resistance to apparently trivial infections. The diabetic condition is usually mild or moderate in degree and the insulin requirement often minimal; control by diet alone may be sufficient. It is in such cases that conservative treatment plays its most important part, especially where impaired myocardial and renal functions are present and may lead to post-operative complications. It has been our experience that limited surgery, aided by chemotherapy and antibiotics, will avoid the necessity for amputation in a large number of these patients. This experience is contrary to the not

uncommon view that amputation, and particularly above-knee amputation, is the only effective surgical treatment.

In most cases infection is not the dominating factor, and widespread infiltration is unusual. The gangrene is slowly progressive and generally remains limited to the area of the foot in which it began.

Treatment

Our routine treatment is as follows: (1) Penicillin or streptomycin is administered systemically, depending upon the organism sensitivity. (2) The state of control of the diabetes is reviewed. Effective and early control is much more easily obtained in these cases than in the primary infective gangrene in the young diabetic. (3) The foot is x-rayed. The presence or absence of bone necrosis is a guide to the extent of surgical treatment.

If there is no necrosis, purely nibbling surgery is performed and the necrotic tissue is thoroughly excised. The part is carefully inspected for deep sepsis, and infected tracks are laid open. Bleeding from the margins and base of the raw area is regarded as a good prognostic omen. The wound is cleansed with hydrogen peroxide, followed by the application of methylated ether. The final dressing is of tulle gras, with or without local penicillin.

If there is radiological evidence of bony changes in the phalanges and metatarsals, then the affected toe or toes with their respective metatarsals are amputated. If possible it is best to amputate through the proximal phalanx rather than disarticulate at the metatarsophalangeal joint, as we have found that disarticulation

has a tendency to impair the blood supply to the adjacent toe, and also that the exposed articular cartilage covering the metatarsal head necroses and delays healing.

Dr. Wilfred Oakley (personal communication) is of the opinion that when amputation of a toe is required there is much to be gained by removing all the other toes of the affected foot at the same time; this avoids troublesome recurrence at a later date. Joslin *et al.* (1946) recommend trans-metatarsal amputation in such cases for the same reason.

From our experience of 50 cases of diabetic gangrene we are profoundly impressed with the excellent results obtained by conservative surgery, especially in those patients with occlusive vascular disease who would normally be described as of the senile arteriosclerotic type. We have found that, provided the devitalized and infected tissues are removed completely and there is free haemorrhage from the edges and base of the area after excision, a satisfactory result with preservation of the limb may be confidently expected.

The accompanying Table shows details of 50 cases which have been treated as described above. A brief record of the first four is given to illustrate the methods which we adopt.

Case 1

A woman aged 70. Diabetic for 13 years, taking soluble insulin, 10 units twice daily. Admitted July, 1949, with a subcuticular abscess on the sole of the right foot, the result of a neglected callus. Blood pressure 210/100. Urine contained albumin ++. Blood urea, 50 mg. per 100 ml.

Procedure.—Incision of the abscess and evacuation of pus: cleansed with hydrogen peroxide and methylated

Details of 50 Cases

Case No.	Age	Sex	Site	Precipitating Factors	Treatment	Follow-up	Result
1	70	F.	R. 3rd toe	Infection and vascular	Amputation	1 year	Satisfactory ambulant
2	61	F.	R. great toe	Infection	Local	2½ years	Satisfactory
3	70	F.	L. 2nd toe, R. great toe	Vascular	Amputation	1½ "	"
4	47	F.	R. 4th toe	"	"	1 year	"
5	65	F.	R. great toe	Infection	Local excision	2 years	Died (coronary occlusion)
6	55	F.	Dorsum R. foot	Infection and vascular	Excision and amputation	1½ "	Died (congestive heart failure)
7	63	M.	R. heel	Infection	Local	3 "	Died (coronary occlusion)
8	58	M.	L. great toe	Infection and vascular	Amputation	3 months	Satisfactory (ambulant)
9	72	F.	L. 2nd and 3rd toes	"	Local	2½ years	Satisfactory
10	51	F.	L. 2nd toe	Infection	"	1 year	Satisfactory (ambulant)
11	57	M.	R. great toe	"	"	4 months	"
12	66	F.	L. 2nd, 3rd, and 4th toes	Vascular	Amputation	1 year	Died (coronary occlusion)
13	62	M.	R. great toe	"	"	3 years	Satisfactory (ambulant)
14	16	M.	Dorsum R. foot	Infection (fulminant)	Local	6 "	"
15	53	F.	R. 3rd, 4th, and 5th toes	Infection and vascular	Amputation	2 "	"
16	66	M.	L. 1st interosseous	Infection (fungus)	Local	3 "	"
17	57	F.	R. 5th toe	Infection	"	4 "	"
18	52	M.	L. 2nd and 3rd toes	"	Amputation	3 "	"
19	75	F.	L. 5th toe	Vascular	"	10 months	Died (congestive heart failure)
20	49	F.	R. 1st interosseous	Infection (fungus)	Local	5 years	Satisfactory (ambulant)
21	60	M.	R. great toe	Infection	"	3½ "	"
22	80	F.	L. 2nd toe	"	Amputation	2 months	Died (senility)
23	63	F.	R. 1st, 2nd, and 3rd toes	Vascular	"	1½ years	Satisfactory (ambulant)
24	69	F.	L. heel	Infection	Local	2½ "	"
25	73	F.	R. 3rd toe	Vascular	Amputation	6 months	"
26	55	F.	R. 2nd toe	Infection	"	2½ years	"
27	44	M.	R. 4th and 5th toes	"	"	3 "	"
28	67	F.	L. great toe	"	Local	1½ "	"
29	71	F.	R. 2nd toe	Vascular	"	5 months	"
30	64	F.	R. 3rd toe	Infection	"	4 years	"
31	77	F.	L. 3rd and 4th toes	"	"	1 year	Died (cerebral haemorrhage)
32	64	M.	R. 2nd toe	Vascular	Amputation	2½ years	Satisfactory (ambulant)
33	53	M.	R. great toe	Infection	Local	5 "	"
34	60	F.	R. 3rd and 4th toes	"	Amputation	4 "	"
35	61	M.	L. 2nd toe	Vascular	"	10 months	"
36	69	F.	R. great and 2nd toes	"	"	3 years	"
37	72	F.	L. plantar	"	Local	1 year	"
38	64	F.	L. 5th toe	Infection	Amputation	1½ years	Died (coronary occlusion)
39	55	M.	R. 1st interosseous	Infection (fungus)	Local	5 "	Satisfactory (ambulant)
40	49	F.	R. great toe	Paronychia	"	2 "	"
41	60	M.	L. 2nd and 3rd toes	Vascular	Amputation	5½ "	Satisfactory (L. hemiplegia)
42	68	F.	R. heel	Infection	Local	1½ "	Satisfactory (ambulant)
43	54	F.	Dorsum L. foot	"	"	2 "	"
44	59	F.	L. 1st toe	Vascular	Amputation	2 "	"
45	57	M.	L. great toe	Infection	Local	8 months	"
46	63	F.	L. 2nd toe	"	"	1 year	"
47	62	F.	R. 4th and 5th toes	Fungus and vascular	Amputation	1½ years	"
48	68	M.	R. 2nd toe	Infection	"	3 "	"
49	71	F.	R. 3rd and 4th toes	Vascular	"	1 year	Satisfactory (R. hemiplegia)
50	62	F.	L. great toe	Infection	"	2 years	Satisfactory (ambulant)

FIG. 1.—Case 1.

ether. Penicillin administered intramuscularly. Wound granulated satisfactorily and patient discharged after 19 days. X-ray film of foot showed "gross arthritic changes with some joint erosion."

Patient readmitted July, 1950, on account of persistent aching and discoloration of the right third toe. X-ray picture was essentially the same as that noted one year previously. The affected toe was removed under general anaesthesia; the wound healed satisfactorily and the patient was discharged after 15 days. She has had no further trouble, and is able to walk unaided (see Fig. 1).

Case 2

A woman aged 61. Diabetic for 15 years, taking soluble insulin, 15 units twice daily. Admitted February, 1949.

FIG. 2.—Case 2.

FIG. 3.—Case 3.

Gangrenous tissue present on the plantar and dorsal aspects of the right great toe with underlying pus. Blood pressure 150/90. There was a marked varicose eczema of the right calf. X-ray picture showed "a little decalcification of the bones of the foot, and calcification of the arteries, but no evidence of bony necrosis." The area was laid open, cleansed with hydrogen peroxide and methylated ether, and dressed with tulle gras. Improvement in this case was rather slow and was interrupted by a localized pocketing of pus; this was drained, and the wound healed satisfactorily. Free bleeding occurred when the tissues were incised, and the prognosis was regarded as good (see Fig. 2).

Case 3

A woman aged 70. Diabetic for two and a half years, taking 6 units protamine zinc insulin daily. Admitted August, 1949, with redness and swelling of right great toe. X-ray picture showed "bony necrosis in the region of the interphalangeal joint."

FIG. 4.—Case 3.

Procedure.—Removal of base of first phalanx and head of first metatarsal, right foot. The metatarsal head was found to be necrotic. Recovery was uneventful, and the patient was discharged a few weeks later. In December, 1949, the adjacent second toe was amputated because of necrosis of the terminal phalanx.

Readmitted January, 1950, with redness and swelling of the second left toe. X-ray film showed "necrosis of the tip of the terminal phalanx." Local amputation of the affected digit was carried out under general anaesthesia. There has been no recurrence, and the patient can walk about unaided (see Fig. 3).

Case 4

A woman aged 47. Diabetic for five years, taking 20 units protamine zinc insulin and 10 units soluble insulin daily. Admitted February, 1950, with swelling and inflammation of the fourth right toe and lymphangitis of the dorsum of the foot. X-ray film showed "erosion of the middle phalanx." Systemic penicillin was administered and the inflammatory condition subsided. No surgical intervention was advised at that time.

Readmitted May, 1950, with recurrence of pain and swelling in the same toe.

Procedure.—Removal of the affected toe under general anaesthesia. Good functional result, and no evidence of recurrence since discharge (see Fig. 4).

The first three patients had all been advised elsewhere to have amputation performed, either of the foot only or at a higher level. All of them are still fully ambulant despite the loss of one or more toes.

Discussion

Are not these results in contrast with those obtained in non-diabetic senile gangrene, which almost inevitably necessitates above-knee amputation? It has been our experience that gangrene in the non-diabetic, even without thrombosis in the main vessels, has not been amenable to treatment by conservative surgery, which can give such encouraging results in the diabetic patient of comparable age. The question thus arises, Why should such a difference exist in patients of similar age and with a comparable degree of vascular degeneration where one is a diabetic and the other not?

The superimposed infection is currently believed to be the dominating factor in diabetic gangrene, and the good results of conservative surgery are attributed to the adequate control of the infection. It is our opinion, however, that the control of the infection is only a secondary factor, and we venture the suggestion that in the diabetic an adequate collateral circulation is already in existence.

It is known that diabetes mellitus predisposes to early degenerative changes in the intima of arteries, and various reasons for this have been suggested, such as increased blood cholesterol and high blood fat, but it is still open to question whether these theories provide the complete explanation. There is no doubt, however, that histological examination of the blood vessels of young diabetics often shows intimal proliferation with deposits of cholesterol crystals and lipid-containing cells. Joslin *et al.* (1946) quote Case 1305, a boy of 16, in whose aorta atheromatous plaques were found; similar findings in young adults are described by Smith (1925) and Oppenheimer and Fishberg (1925).

Joslin and his colleagues hold the view, and our own results support it, that the slowly progressive occlusion of the vascular lumen stimulates the development of collaterals in the limb. When, therefore, complete obstruction occurs in the smaller vessels, this collateral

circulation maintains satisfactory nutrition in the neighbourhood. Control of infection in the affected toe, either by simple débridement and drainage or by local amputation, will prevent spread to adjacent parts and thus hinder thrombosis in vessels which are still patent.

On the other hand, the non-diabetic with senile medial sclerosis, who suddenly develops a thrombus in one of the large vessels, has no compensatory mechanism, and so widespread necrosis takes place below the level of the obstruction.

Summary

Gangrene in the diabetic is extremely amenable to conservative surgery, and a radical amputation should never be performed as a routine measure. The theory is advanced that, although control of infection of the gangrenous tissue is of paramount importance, the diabetic state stimulates the formation of a collateral circulation which is usually well established when the crisis of peripheral vascular thrombosis supervenes.

We should like to express our thanks to Professor A. M. Boyd, Department of Surgery, Royal Infirmary, Manchester, for his helpful criticism and encouragement in the preparation of this paper.

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ASSOCIATED PERFORATION AND HAEMORRHAGE IN PEPTIC ULCERS TREATMENT BY IMMEDIATE GASTRECTOMY

BY

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While perforation and haemorrhage are both common complications of peptic ulceration, they do not, fortunately, often occur simultaneously. Gordon-Taylor (1937) has classified these associated disasters into three groups: (1) haemorrhage and perforation occurring concomitantly, (2) haemorrhage following a recently treated perforation, and (3) perforation occurring after haemorrhage.

I wish to report three recent cases which fall into the first group and in which the two complications presented together. Case 3 is unusual in the pathological findings.

Case 1

A man aged 40 was admitted as an emergency on May 22, 1950, having had a sudden onset of generalized abdominal pain six hours previously. He had vomited several times in the interval and brought up "coffee grounds." A five-year history suggestive of peptic ulceration was obtained, and clinically he presented characteristic features of a perforated peptic ulcer. In addition he was very shocked and showed marked pallor. His blood pressure was 100/? mm. Hg, the radial pulse was of poor volume, and the peripheral circulation showed signs of collapse. A Ryle's tube obtained altered blood from the stomach. Pre-operatively 2 pints (1.14 litres) of blood was given followed by plasma, and two hours later his general condition had improved, his blood pressure rising to 120/90 mm. Hg.

At operation, under general anaesthesia, a perforated ulcer was found on the antero-superior aspect of the first part of the duodenum. The peritoneal cavity was full of