



Diabetes mellitus is a common and important clinical problem in the urbanized Johannesburg African. A survey of Africans aged 30 and over attending the Baragwanath Hospital Casualty Department showed an incidence of diabetes of about 1%.<sup>1</sup> Yet, apart from Campbell's studies<sup>2,3</sup> on the Zulu diabetic, a search of the literature yielded little of note on diabetes in the South African Bantu. We have therefore undertaken an analysis of the records of 250 new cases of diabetes mellitus in African subjects admitted to Baragwanath Hospital during the period 1951-1957. These cases were selected at random and constituted at least 75% of all the new African diabetics admitted during this period.

#### ANALYSIS OF PERSONAL HISTORY

##### *Age at Onset and Sex*

There were 154 females and 96 males, a female predominance of 1.6:1. The distribution according to sex and age at the onset of the disease is shown in Fig. 1.

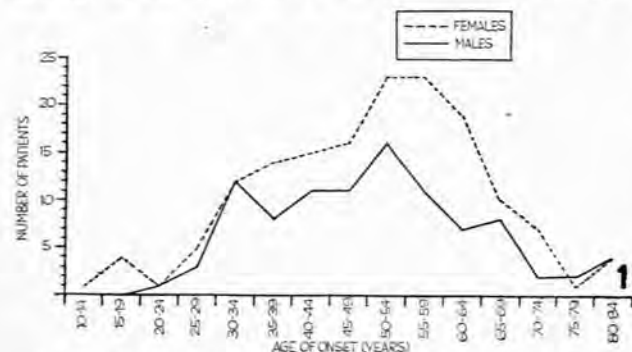


Fig. 1. Age and sex distribution of 250 African diabetics.

The majority of the patients (75.6%) were more than 40 years old when they first became ill, the peak incidence for both sexes being in the sixth decade. There was no case below the age of 12 years.

Among the patients under the age of 40 in whom constitution was specified, obese patients equalled in number those of thin or average build, while over this age obese patients predominated in a ratio of 2.7:1. Patients under the age of 40 had a higher incidence of ketosis (38%) than those over 40 (19%). The ratio of females to males was approximately the same in the age groups above and below 40.

##### *Constitution*

Constitution was specified in 184 patients (121 females

and 63 males), 124 (67%) being described as obese and 60 (33%) as either thin or of 'normal', 'average' or 'medium' build. About three-quarters of the females and one-half of the males were obese.

These findings, based as they are on only a part of the total series and on the arbitrary assessment of constitution by a large number of different observers, must obviously be treated with reserve. However, an investigation of the constitution of 107 African diabetics currently attending the diabetic clinic at Baragwanath Hospital yielded essentially similar results (unpublished observations).

Of the obese patients 80% were over the age of 40, the ratio of females to males was 2.8:1, and the incidence of ketosis was 13%. The non-obese patients were more or less equally distributed between the different age groups, the ratio of females to males was 1:1, and the incidence of ketosis was 32%.

##### *Occupation*

The occupations have been divided into 2 broad categories: skilled (teachers, nurses, ministers of religion, business men, clerks, and artisans) and unskilled (manual labourers). The occupation was specified in 243 cases. Of these 14.8% were skilled workers. This is more than twice the number, 6.8%, found in a control group of admissions (100 males and 150 females). Of the male diabetics 24.7% were employed in skilled occupations as compared with 11% of the male controls. The corresponding figures for females were 8.7% and 4%.

##### *Tribal Distribution*

Sothos and Zulus, in about equal numbers, accounted for 60% of the cases. The remainder were distributed among 14 other tribes, mainly Xhosa, Tswana, Swazi, and Ndebele. A control series of 250 non-diabetic admissions to Baragwanath Hospital showed a similar tribal distribution.

##### *Parity*

In 59 postmenopausal diabetics parity was specified. These patients had a total of 334 children, an average parity of 5.66. A control group of 100 postmenopausal females drawn from a house-to-house survey in 2 Johannesburg African townships had an average parity of 5.65.<sup>4</sup> It is possible, however, that the parity for the diabetic women is an underestimate since in some cases stillbirths and deceased children might have been omitted from the case records.

##### *Duration of Diabetes before Diagnosis*

This was determined from the duration of the classical symptoms of diabetes (defined below). Information on only 131 cases (64 males and 67 females) was available. The

reason for this was that more than two-thirds of the total number of cases in the series presented with some complication of diabetes and specific enquiry into the duration of illness was frequently confined to the complication as opposed to the classical diabetic symptoms.

Two-thirds of the 64 males were admitted within 2 months of the onset of symptoms, whereas about one-quarter of the 67 females presented within this time. Only 11% of the males gave a history lasting longer than 1 year as opposed to 33% of the females.

#### MODE OF PRESENTATION

The different modes of presentation are summarized in Table I.

TABLE I. MODE OF PRESENTATION OF 250 AFRICAN DIABETICS

Presentation	Number presenting	% of patients
Classical symptoms only	54	21.6
Diabetic complications	181	72.4
Eye complications	61	24.4
Ketosis	53	21.2
Infection	40	16.0
Cardiovascular complications	9	3.6
Neurological complications	6	2.4
Miscellaneous complications	12	4.8
Incidental	22	8.8
	257*	102.8

\* The excess over 250 is accounted for by 7 patients who presented with 2 complications each.

It will be noted that about 70% of the total number of cases in the series presented with one or more of the recognized complications of diabetes.

#### Classical Symptoms

By classical symptoms is meant polydipsia, polyuria, polyphagia, weight loss, and weakness. Only patients who volunteered one or more of these as the main complaint and who were free of any of the complications of diabetes are considered to have presented with classical symptoms. There were 54 (21.6%) such patients, 25 males and 29 females. In a further 106 patients classical symptoms were elicited. Thirteen patients (9 females and 4 males) presented with pruritus. In 7 of the females the pruritus was vulval.

#### Ketosis

In this analysis ketosis designates a state characterized by marked ketonuria, acidotic breathing and severe dehydration, with in most cases some degree of impaired consciousness.

Fifty-three patients (21.2%) presented with ketosis. A further 6 patients did not have ketosis on their first admission to hospital but presented with this complication on a subsequent admission. Of these 59 ketotic patients there were 27 males and 32 females. Thus 28% of the males in the series developed ketosis as compared with 20.7% of the females.

The patients in the ketotic group were younger than the patients in the series as a whole. Of the ketotic patients 40% (23 cases) were under 40 years, 44% (26 cases) were between 40 and 60 years and 16% (10 cases) were over the age of 60. In the whole series the corresponding figures were 25%, 50% and 25%.

Of the 35 ketotic patients in whom constitution was recorded, 19 (54%) were described as thin or of average build, and 16 (46%) as obese. Of the 184 cases with specified constitution drawn from the series as whole, 33% were thin or average, and 67% were obese.

Infection, mainly pulmonary, renal and cutaneous, was an additional complication in 18 (30%) of the ketotic patients. In 4 of these the patients presented with symptoms referable to both the ketosis and the infection but in the remainder the infection was discovered on examination or at necropsy.

Of the 53 patients who presented with ketosis on their first admission to hospital, 24 died. All but 1 of these died during

this admission, the remaining patient dying after repeated admissions with ketosis. Of the 6 patients who presented with ketosis on a subsequent admission, 1 died.

Of the 25 ketotic patients who died (Table II, cases 1-25), 20 were aged 40 or more. This represents 55% of the ketotic patients in this age-group. By comparison, the mortality rate for ketotic patients under the age of 40 was 22%.

It is clear that ketosis is a common and serious complication in the African diabetic. There appear to be 2 main reasons for this high mortality. Firstly, there is the late presentation. Of the 25 ketotic patients who died, 7 were in coma on admission to hospital, 8 were in semi-coma, 6 were stuporose or mentally confused and only 4 were conscious and rational. In several instances the disturbance of consciousness had commenced 12, 24 or even 36 hours before admission. The reasons for this are mainly socio-economic and with improved living standards, educational and medical services for the African, such late presentations should become less frequent.

Secondly, in 14 of the 25 cases the ketosis was associated with some other complication which might have contributed to death. In 11 cases the additional complication was infective and in 2 it was thrombo-embolic, while the remaining case had cirrhosis of the liver with bleeding from ruptured oesophageal varices. (This latter case is described in detail under 'Deaths'). Some of these complications were probably consequences of the ketotic state, such as bronchopneumonia developing in the comatose patient, or venous thrombosis occurring with severe dehydration and hypotension; in other cases the additional complication may have served to precipitate or aggravate the ketosis.

Of the 36 ketotic patients who were discharged, about two-thirds required readmission, the main reasons being further episodes of ketosis, hypoglycaemic attacks and restabilization.

In 33 patients the insulin dosage on discharge was known. Twelve (9 males) needed more than 75 units of insulin daily, 10 (5 males) between 50 and 75 units and 11 (3 males) less than 50 units. Among the 8 women who needed less than 50 units a day there were 2 who required less than 25 units and 1 who was controlled on diet alone. It would appear that the stabilization dose of insulin is greater for the male ketotic than for the female.

#### Infection

Forty patients (16%) presented with symptoms referable to infection. Fifteen had pyogenic infections of the skin, and 14 pulmonary infections (3 of which were tuberculous), while the remainder manifested a variety of infections. A further 33 patients, although not presenting as such, were found to have an infection on examination. The majority of these (19 cases) had pyuria of varying degree. Of the remainder, 6 had pulmonary infections of which 4 were tuberculous, and 7 had pyogenic or fungal skin infections.

#### Eye Complications

Sixty-one (24.4%) patients presented with disturbances of vision. Of these, 49 had cataracts, 1 glaucoma and 1 optic atrophy. In the remainder no obvious cause could be discovered for the visual disturbance which was presumably due to metabolic changes in the lens. In a further 10 patients who presented with cerebrovascular accidents, infections or ketosis, cataracts were found on examination. Finally, there were 3 patients in whom cataracts were not observed on the first admission but were discovered on a subsequent admission.

Of these 62 cases with cataracts, 30 were over the age of 60, 28 were between 40 and 60, and 4 were under 40, the youngest being a female aged 17.

#### Cardiovascular Complications

Eight patients presented with cerebrovascular accidents due to haemorrhage or thrombosis and 1 with peripheral vascular disease and gangrene. On examination, 6 patients were found to have diabetic retinopathy, including 1 with massive albuminuria and hypertension. In no case was coronary artery disease detected.

In 74 patients (52 females and 22 males) the diastolic blood pressure was greater than 90 mm.Hg. In 44 patients the diastolic pressure was between 90 and 110, in 22 between 110 and 130 and in 8 between 130 and 150 mm.Hg. The majority of the hypertensive diabetics were over the age of 40 years.

Neurological Complications

Three patients presented with peripheral neuritis, 2 with myelopathy and 1 with impotence. Seven further patients were found on examination to have peripheral neuritis.

Miscellaneous

Twelve patients presented with a variety of other possible diabetic complications: stillbirths or dystocia due to large infants (6 cases), menstrual disturbance (4 cases), cholelithiasis (1 case) and necrobiosis lipidica diabetorum (1 case).

Incidental

In 22 cases (8.8%) the diabetes was discovered on routine examination of the urine, the patients presenting with symptoms totally unrelated to diabetes mellitus or its complications.

THERAPY ON DISCHARGE

The therapy on discharge was known in 225 patients. Diet alone controlled 14%, while 13% required between 5 and 25 units of insulin daily, 38% between 25 and 50 units, 19% between 50 and 75 units and 16% more than 75 units. Of the 32 patients controlled on diet alone, 27 were females. On the other hand, of the 35 patients requiring more than 75 units of insulin daily, 22 were males.

READMISSIONS

In the period under review 58 cases (23.2%) required readmission on 108 occasions. The reasons for readmission were hypoglycaemia due to insulin overdosage (32), restabilization (29), ketosis (16), infections (17), cataract extraction (6), injection abscesses (2), complications of pregnancy (3), and miscellaneous (3). One of the hypoglycaemic episodes resulted in permanent brain damage with dementia.

DEATHS

Thirty-four diabetic cases (23 females and 11 males) died at Baragwanath Hospital in the period reviewed. It is probable that there were further deaths at home and at other hospitals. The causes of death are summarized in Table II.

The predominant importance of ketosis is clear, being

TABLE II. CAUSE OF DEATH IN 34 AFRICAN DIABETICS

				Cause of death		
No.	Age	Sex	Constitution	Clinical assessment	Autopsy findings	Cause of death
1	30	M	Medium	Ketosis	Pulmonary infarction and femoral vein thrombosis	
2	30	F	Obese	Ketosis	—	
3	38	F	Thin	Ketosis	Bronchopneumonia	
4	38	F	—	Ketosis	—	
5	39	F	Obese	Ketosis	Acute bronchitis and cystitis	
6	40	M	Thin	Ketosis	Nil contributory	
7	40	M	—	Ketosis	—	
8	42	F	Obese	Ketosis. Cirrhosis of the liver and ruptured oesophageal varices	Septal cirrhosis, varices, and marked siderosis of the liver, pancreas, spleen, heart, and stomach	Generalized atherosclerosis, but no evidence of organ infarction
9	45	F	Thin	Ketosis	Acute dilatation of the stomach	
10	47	F	Obese	Ketosis	—	Bronchopneumonia and subacute pyelonephritis
11	48	F	Obese	Ketosis. Fibroids	—	Fibroids with bilateral hydronephrosis and cystitis
12	50	M	Obese	Recovery from ketosis followed by 3rd nerve palsy and contralateral hemiplegia	—	Mucormycosis with thrombosis of cavernous sinus and adjacent carotid artery
13	51	M	Medium	Ketosis	—	Nil contributory
14	52	M	Medium	Ketosis	—	Acute suppurative pyelonephritis
15	57	F	Obese	Ketosis. Pneumonia	—	—
16	57	F	Obese	Ketosis	—	—
17	60	M	—	Ketosis. Pulmonary embolism	—	—
18	62	F	Medium	Ketosis. Septic gangrene of right foot	—	Gangrene of right foot and calf
19	64	M	Obese	Ketosis. Anuria	—	—
20	67	M	Thin	Ketosis. Pneumonia	—	—
21	69	F	Thin	Ketosis. Gas gangrene of buttock	—	—
22	70	M	—	Ketosis	—	—
23	80	F	Thin	Ketosis	—	Bronchopneumonia and cystitis
24	82	F	Medium	Ketosis	—	—
25	50	F	—	Ketosis	—	Nil contributory
26	30	F	Obese	Large abscess of back complicated by ketosis	—	—
27	60	F	—	Stage IV carcinoma of the cervix complicated by ketosis	—	—
28	55	F	Obese	Gangrene of the leg; midhigh amputation with postoperative hypoglycaemia	—	—
29	55	F	Thin	Hypoglycaemia. Nodular hepatomegaly	—	—
30	66	M	Thin	? Hypoglycaemia. 'Haemochromatosis' with liver failure	—	Septal cirrhosis and marked siderosis of liver, pancreas, spleen, heart, adrenal, thyroid, and stomach
31	42	F	Thin	Bilateral cavitating pulmonary tuberculosis	—	—
32	65	F	Obese	Cerebral haemorrhage	—	—
33	57	F	Thin	Cause of death obscure. Peripheral neuritis clinically	—	—
34	50	F	Thin	Cause of death obscure. Admitted for stabilization	—	—

Cause of death

Clinical assessment

Autopsy findings

associated with 27 of the 34 deaths. In 25 cases it occurred as the presenting feature while in the remaining 2 it complicated the course of some other presenting condition—a large abscess on the back and a stage IV carcinoma of the cervix.

Of the 7 non-ketotic deaths, 2 were due to hypoglycaemia, 1 was possibly due to hypoglycaemia in a patient with liver failure (*vide infra*), 1 was due to pulmonary tuberculosis, and 1 to cerebral haemorrhage, while in the remaining 2 the cause of death was obscure. Both hypoglycaemic deaths occurred in hospitalized patients receiving insulin. The first occurred in the postoperative period following a mid thigh amputation for gangrene of the leg. In the second case hypoglycaemia developed in a patient, with an enlarged nodular liver, whose insulin requirements varied markedly.

Two cases which came to necropsy are of particular interest. The first (Table II, case 8) was admitted in semi-coma, no history being available. Examination revealed an obese, dehydrated, pale and jaundiced female with acidotic breathing. The liver was enlarged 5 fingerbreadths below the costal margin and the lower limbs were moderately oedematous. On rectal examination a melaena stool was observed. Shortly after admission the patient had 3 episodes of Jacksonian epilepsy involving the right upper limb. The blood sugar was 600 mg. per 100 ml. and the urine contained glucose + + + +, and acetone + + + +. A diagnosis of diabetic coma, cirrhosis of the liver, and ruptured oesophageal varices was made. On therapy the ketosis, dehydration and anaemia were largely corrected but the patient remained semi-comatose. She continued in this state for 3 days and then died after a massive haematemesis. Necropsy showed a septal cirrhosis and heavy deposits of iron in the liver, pancreas, heart, gastric mucosa, and spleen.

The second case (Table II, case 30), was admitted with backache following the lifting of a heavy weight and the diabetes was discovered on routine urine testing. In addition the patient was found to have a 4-finger enlargement of the liver, ascites, oedema of the lower limbs, and slight jaundice. A diagnosis of haemochromatosis was made. The patient was stabilized with insulin and discharged about 4 weeks after admission. Over the next 4 months he was readmitted on several occasions, 3 times for the relief of ascites and twice for hypoglycaemia. On the final admission the patient was extremely emaciated, but only moderate ascites was present. The blood sugar was 300 mg. per 100 ml. Eighteen hours after admission the patient died suddenly. The reason for this was not apparent but it may have been due to hypoglycaemia since he was given 20 units of soluble insulin 12 and 6 hours before death. Necropsy revealed a septal cirrhosis of the liver, heavy deposits of iron in the liver, pancreas, spleen, heart, adrenal, thyroid, and gastric mucosa, and slight deposits in the testes and the parotid glands.

These 2 cases thus resemble the classical picture of idiopathic haemochromatosis as described by Sheldon,<sup>5</sup> and are discussed later.

Apart from these 2 cases the pancreas was examined histologically in 7 cases. In 6 it was described as normal and in 1 slight atrophy of the acini was noted.

#### DISCUSSION

The principal characteristics of diabetes mellitus in the urbanized Johannesburg African, as shown by this study, may be summarized as follows:

The disease was commoner in females but appeared to be more severe in males as judged by their more acute onset, their higher insulin requirements on discharge from hospital and, possibly, their greater tendency to develop ketosis. The onset of the majority of cases occurred over the age of 40. No case was found below the age of 12 years. When compared with a control population a significantly greater number of African diabetics was employed in skilled occupations.

Of the cases over 40 the majority were obese and the incidence of ketosis was 19%. Those under 40 were thin, fat, or of average build and the incidence of ketosis was 38%.

About 70% of the patients presented with one of the recognized complications of diabetes—ketosis, infections, and cataracts accounting for the majority of the presentations. Ketosis was the major cause of death. By contrast myocardial infarction was absent and diabetic retinopathy, nephropathy and peripheral vascular disease were uncommon. Hypertension was frequently found but it has still to be established whether the incidence is greater than that in non-diabetic Africans.

The rate of readmission was high, the principal reasons for which were hypoglycaemic attacks, restabilization, ketosis and infection.

#### Other Series

The only other large series of Bantu diabetics investigated in South Africa is that of Campbell,<sup>2,3,6</sup> who studied Zulu diabetics in Durban, Natal. These diabetics are in the main similar to our own. About two-thirds of Campbell's cases were middle-aged, mostly overweight and insulin resistant; one-quarter were under 40, usually thin and liable to ketosis on withdrawal of insulin, while the remainder were classified as senile or peasant diabetics. The senile diabetics were generally over 60 years at onset and thin, and they usually presented with cataracts and lived in rural areas. By contrast, most of the young and middle-aged Zulu diabetics were town-dwellers. The pattern of complications was similar to that of our own cases. As regards therapy, Campbell found that his obese patients responded well to diet if this could be imposed, and also to oral antidiabetic drugs where dietary control was not possible.

In White subjects Lawrence<sup>7</sup> showed that diabetics are largely divisible into 2 types—the young, thin, insulin-sensitive diabetic who readily becomes ketotic when insulin is withdrawn, and the middle-aged, obese, insulin-resistant diabetic in whom ketosis is relatively uncommon. The urbanized African diabetic can, by-and-large, be similarly classified. He differs from the White diabetic principally in respect of the incidence of the vascular complications

of diabetes. In White subjects vascular disease constitutes the major diabetic complication. Of 656 deaths in diabetic subjects over the period 1950-1952 at the Joslin Clinic, USA, about three-quarters were due to vascular disease, mainly myocardial and cerebral infarction and diabetic nephropathy.<sup>8</sup> The reason for the low incidence of vascular disease in the African diabetic is unknown. It may be that in the African the diabetic syndrome is of relatively recent origin, its development being related, for example, to urbanization (*vide infra*) and that with time vascular disease may become increasingly manifest. The rarity of myocardial infarction may be related to the immunity which Africans in general exhibit towards this complication.

#### AETIOLOGY

Apart from such factors as age, sex and constitution, our analysis points to 2 factors as being aetiologically significant.

##### 1. Siderosis

In 2 of the patients who died necropsy revealed a septal cirrhosis of the liver associated with heavy deposits of iron in the liver, spleen, pancreas, heart and gastric mucosa; in 1 of the cases there were heavy deposits in the thyroid and adrenal glands as well.

There are 2 possible explanations for these findings. Firstly, that the cases are examples in Africans of idiopathic haemochromatosis as classically described by Sheldon.<sup>9</sup> Secondly, that they represent in *extreme* degree the siderosis which is so common in South African Bantu of both sexes.<sup>9-11</sup> The qualification 'extreme' is necessary since in the average case of Bantu siderosis, the iron deposits are found mainly in the liver and reticulo-endothelial system; the heart, pancreas and other epithelial tissues are usually spared. It is suggested that in extreme cases the iron may be present in these tissues as well.

To decide between these 2 possibilities we may consider the data provided by an autopsy study on 20 African diabetics who died between 1954 and 1959.<sup>12</sup> Of these 20 cases, 4 (including the 2 described above) were found which were characterized by septal cirrhosis of the liver and heavy deposits of iron in the liver, spleen, heart, pancreas, and other epithelial tissues. Analysis of the 4 cases pointed strongly to their being extreme examples of Bantu siderosis rather than cases of idiopathic haemochromatosis. Firstly, if they were cases of idiopathic haemochromatosis, the number found in the autopsy series (20%) would suggest an incidence of idiopathic haemochromatosis far in excess of that described elsewhere. Secondly, 3 of the 4 cases were females; idiopathic haemochromatosis is a condition found predominantly in males. Thirdly, chemical analysis showed concentrations of iron in the spleen in all 4 cases which were considerably greater than those described in idiopathic haemochromatosis but which were similar to those found in Bantu siderosis.

##### 2. High Living Standards and Urbanization

Compared with a control population, a significantly greater number of our diabetics were found to be employed in skilled occupations. Campbell<sup>2,6</sup> made a

similar observation in his Zulu patients and showed that the diet consumed by his skilled diabetics was similar to that of White South Africans apart from a slightly higher carbohydrate intake.

The diabetics in our series were drawn from Johannesburg and the surrounding African townships. Similarly, Campbell's cases were mostly city-dwellers. That the process of urbanization is significantly related to the development of diabetes, is suggested by Campbell's<sup>2</sup> observation that in the obese, middle-aged Zulu diabetic (the commonest type of diabetic seen by him), there was a remarkably constant period of exposure to city life (about 20 years) before the disease became manifest.

There is also the evidence, based on survey studies,<sup>1,13</sup> that the incidence of diabetes in the urbanized Johannesburg African female is considerably greater than that of the rural Basuto female. The male incidence in the 2 populations was similar. However, the number of rural Basuto males surveyed was relatively small and it is possible that a more extensive study may show that, for males also, the urban incidence of diabetes is greater than the rural.

#### SUMMARY

An analysis of 250 cases of diabetes mellitus in the urbanized Johannesburg African is presented.

The disease was commoner in the female and in the majority of cases the onset occurred over the age of 40. In this age-group the majority of patients were obese and the incidence of ketosis was 19%. Patients under the age of 40 were of variable constitution and the incidence of ketosis was 38%.

About 70% of the cases presented with one of the recognized complications of diabetes—ketosis, infection, and cataracts accounting for the majority of presentations. Ketosis was the commonest cause of death. By contrast vascular disease, myocardial infarction in particular, was uncommon.

Attention is drawn to the possible aetiological significance of rising living standards, urbanization and siderosis.

We thank Dr. I. Frack, Superintendent of Baragwanath Hospital, for permission to publish.

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