

# Some Statistical Investigations in Diabetes Mellitus

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The purpose of the statistical investigations discussed in this paper was to elucidate among known diabetic subjects: (1) the age group at which the female predominance is especially manifest; (2) the age group at which "diabète maigre" and "diabète gras" occur; (3) the frequency of "diabète maigre" and "diabète gras" in males and females; (4) the significance of the number of pregnancies and of obesity as promoting factors in the pathogenesis of diabetes mellitus; (5) the cause of the female predominance.

The investigations are based on the data available from patients visiting the outpatient department for diabetes of the Clinic for Internal Diseases, University Hospital of Groningen. This is a free clinic. On Jan. 1, 1956, a total of 773 male and 1,379 female patients were under treatment, all from the three northern provinces of the Netherlands. They may be considered as representative of this part of the country.

The visitors to the outpatient department are older than twelve years. There is no further selection regarding the severity of the diabetes, sex, or age at which they come under treatment and time of onset of the diabetes. Most, however, are treated from the beginning of the disease, and then remain under regular inspection. The aim of the treatment with diet or with diet and insulin, is to reduce the blood sugar content to values below 200 mg. per 100 ml., to decrease the glucosuria to minimal amounts, to avoid acetonuria and to prevent hypoglycemia. At first, obese diabetics are treated by reducing the caloric intake to about 1,200 calories, since it is well known that an adequate weight reduction considerably improves carbohydrate tolerance.

Figure 1 represents the age distribution of the patients. This more or less corresponds with that found in other clinics. In contrast to the findings of Spiegelman and Marks,<sup>1</sup> who found a marked predominance of females as early as after the twenty-fifth year (20 per

cent between twenty-five and thirty-four years and 100 per cent between forty-five and sixty-four years), in our clinic the number of male patients younger than forty is somewhat higher than that for the females. Over forty there is the traditional marked predominance of women.

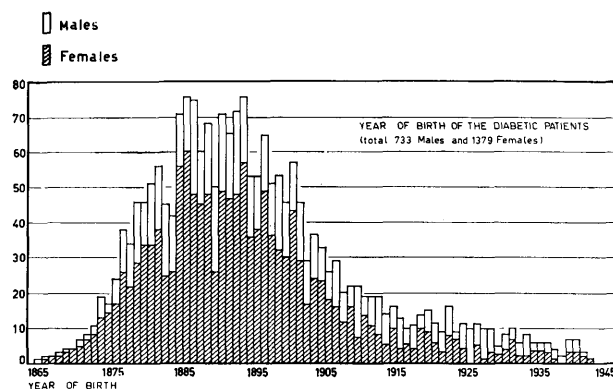


FIGURE 1

Based on data from the English Bureau of Statistics, Pyke demonstrated that with aging a surplus of women develops naturally among the population as a whole.<sup>2</sup> This also holds true for the Netherlands, although not to the same degree as in England (see table 1). The data for the Netherlands for 1953 were provided by the Dutch Central Bureau of Statistics (The Hague).

TABLE 1  
Number of females per 100 males

Age group	England Pyke	The Netherlands	Diabetics Diabetes Clinic Groningen absolute figures
0-14		95	
15-19		96	63 (16 males— 10 females)
20-29		101	74 (46 " — 34 " )
30-39		102	95 (60 " — 57 " )
40-49	100 (45-49)	105	114 (90 " —103 " )
50-59	110	105	214 (141 " —302 " )
60-69	131	107	222 (199 " —442 " )
70-79	149 (and older)	119	292 (26 " — 76 " )

From the Clinic for Internal Diseases of the State University of Groningen, Netherlands. Director: F. S. P. van Buchem, M.D.

Table 1 shows that the predominance of female diabetics in the groups fifty years of age and older can certainly not be explained from the natural surplus. (The deviations with regard to the proportional figures in the whole Dutch population are not significant for the groups below age fifty (at 5 per cent level), but they are very significant higher than age fifty). The causes usually mentioned are that more women are obese, that they have a less active way of living, and that the menopause may be of influence (Joslin et al.).<sup>4</sup> We shall revert to this later.

Pyke<sup>2</sup> believed that he demonstrated a relationship between pregnancies and incidence of diabetes mellitus. The chance of developing diabetes would appear greater with increasing parity. We investigated this relationship in a group of 299 married women in whom diabetes had developed after forty-five years of age (table 2). This table gives a comparison of the percentages of the 299 diabetic subjects with various numbers of children, with the corresponding percentages of the Dutch women as a whole in 1947 and who were married before 1918, therefore we consider these comparable groups. As in Pyke's investigation, only the live births are included in the table. Unfortunately the number of stillborn is unknown in both groups. Our data were provided by the Central Bureau of Statistics (The Hague).

TABLE 2

Number of children	Normal 423,797= 100 per cent	Married women 299=100 per cent	diabetics absolute figures
0	8.12	7.69	23
1	8.45	8.03	24
2	14.98	17.39	52
3	14.14	12.37	37
4	11.78	14.38	43
5	9.42	8.70	26
6	7.63	7.36	22
7	6.19	6.69	20
8	5.17	4.68	14
9	4.15	6.35	19
10 or more	9.98	6.35	19

Table 2 shows at a glance that there is no correlation between the incidence of diabetes and the number of children. This impression was confirmed by calculating chi-square at 5 per cent level.

Figure 2 gives a survey of the duration of diabetes from the time of diagnosis in 716 males and 1,331 females. Most of the patients had had diabetes for less than ten years. This can partially be explained from the marked rise in the number of diabetic patients who have visited the outpatient clinic since 1946. The steady yearly increase of the number of patients beginning in 1920, was interrupted during the years 1940-45, espe-

YEAR IN WHICH THE DIABETES BECAME MANIFEST  
(total 716 Males and 1331 Females)

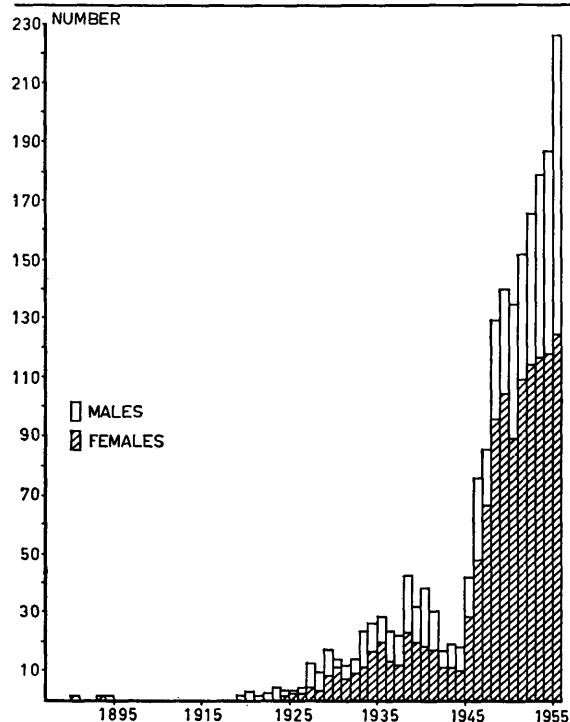


FIGURE 2

cially during 1943-45. This was probably due to World War II, food being scarce especially from 1943 to 1945, as it is known that a limited supply of calories exerts a favorable influence on the pathogenesis and severity of diabetes; this was noticed by Bouchardat as early as 1870 during the siege of Paris.

The correlation between use of insulin, age and year of onset of the diabetes, as determined for the men, is shown in figure 3. This indicates that most of the older patients can be regulated with diet only, especially during the first five years. Then there is a gradual rise of the quantity of insulin required, which is, however, usually moderate. Only a few of the younger patients are able to get along on a controlling diet alone; most need insulin from the beginning with the daily requirement rising rapidly as a rule.

According to Labbé, a distinction may be made between "diabète maigre" and "diabète gras." The latter form of diabetes is attended by obesity and occurs especially in adults over thirty years of age. Satisfactory regulation of the diabetes is usually obtained with a low-calorie diet, and then the carbohydrate tolerance generally improves. These patients usually show a striking insensitivity to insulin and diabetic coma occurs only rarely in them. The "diabète maigre" is attended by a

SOME STATISTICAL INVESTIGATIONS IN DIABETES MELLITUS

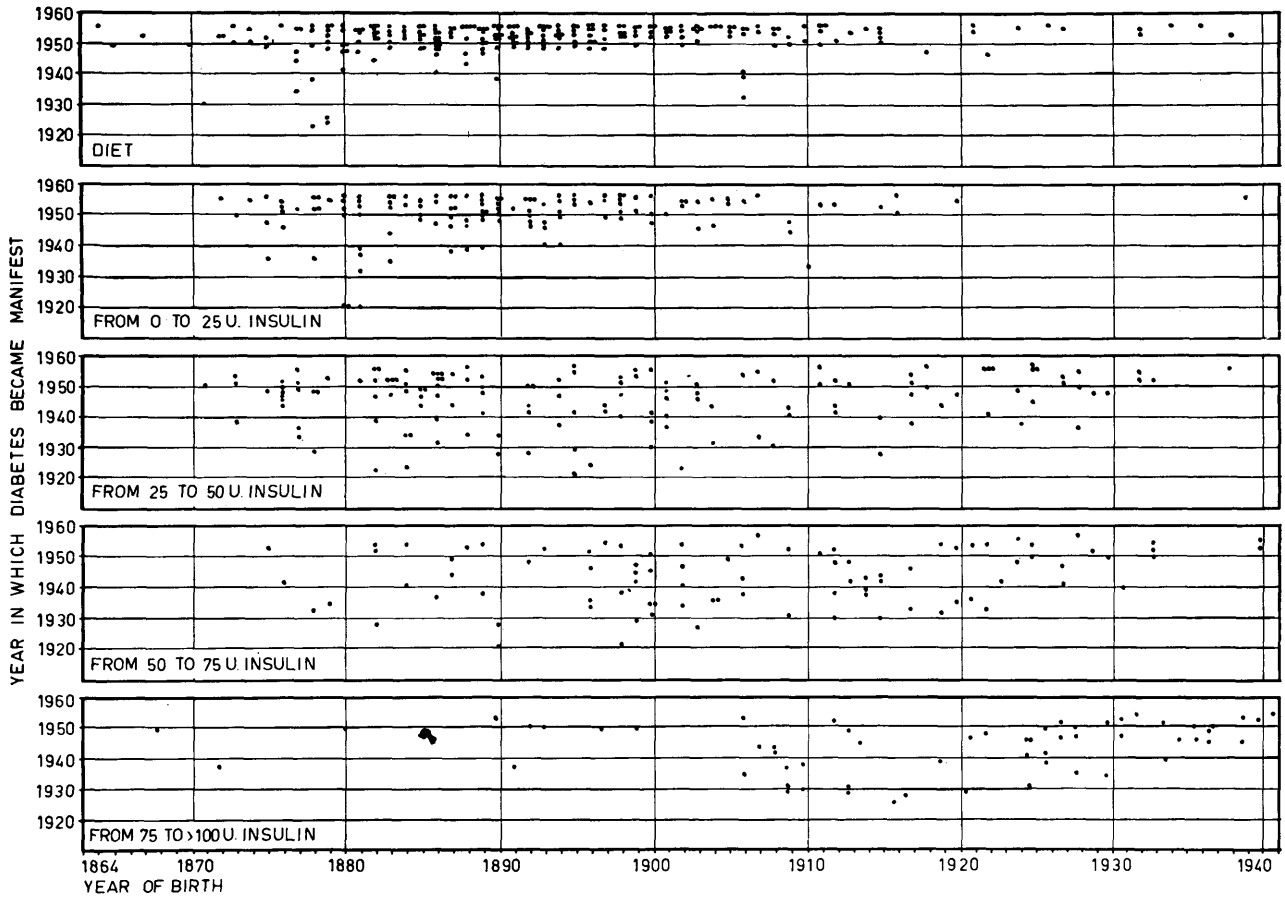


FIGURE 3

low body weight and occurs more frequently in the younger patients. These patients have to be treated with insulin and they react well to it. They have a far greater tendency to develop diabetic coma.

In "diabète gras" there would appear to be rather decreased sensitivity to insulin, in contrast to "diabète maigre" in which a deficiency of endogenous insulin is said to exist. This theory is supported by the findings of Bornstein.<sup>6</sup> In fifteen patients of the latter category he was unable to demonstrate insulin in the plasma, while he found it in thirteen patients with obesity without acidosis (0.10-0.32 mU/ml.). In normal people he found 0.24-0.40 mU/ml.

Our patients of whom height, body weight and age were recorded in our clinic at the beginning of the disease, are divided into three groups according to weight: overweight (D), with normal weight (N) and underweight (M). This division is not easy because we have insufficient data for normal weight in the Dutch population by age, height and sex.

We used the tables given by Duncan,<sup>3</sup> which agree roughly with those of Pett and Ogilvie (in Brozek).<sup>5</sup>

Thin persons under forty-five years were considered those weighing less than the average by 3 kg. or more, as indicated for the given height, sex and age. The overweight weighed 3 kg. or more above the average. For patients over forty-five the range of variation of 5 kg. above or below the average was taken as normal, because the "normal" variation seems to be greater. Moreover, if we had taken a smaller range of variation, the figures would be even more favorable to our conclusions.

Accordingly the data of 482 men and 921 women were collected and represented in figure 4. It appears that "diabète gras" is especially a disease of the females (57.11 per cent) and that it occurs far less frequently in males (21.58 per cent). It therefore seems probable that the predominance of the female diabetics is especially connected with the obesity. We would have more certainty about this if the weights of males and females of the whole population, subdivided in the same way, were known to us.

Figure 5 shows the age of onset of diabetes for men and women, classified according to "diabète maigre" and "diabète gras." "Diabète gras" as a rule does not appear

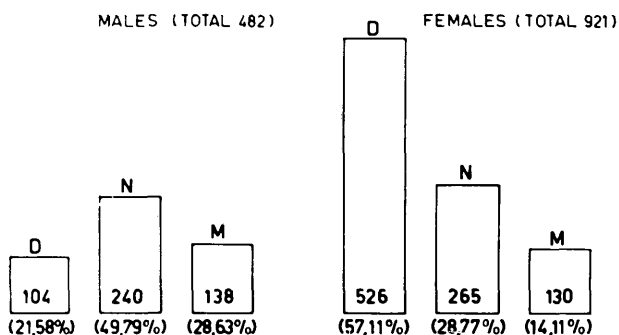


FIGURE 4

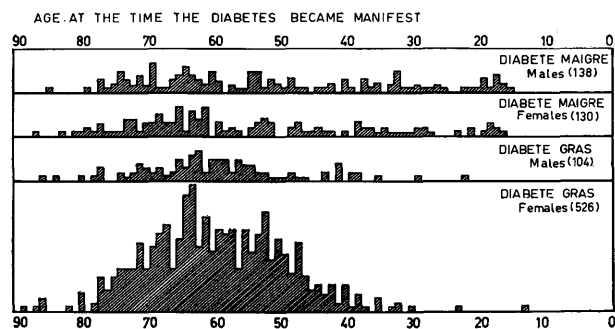


FIGURE 5

until the thirtieth year of life, in contrast to "diabète maigre," which may occur in youth as well as in older persons. This holds true for both men and women. The young diabetics therefore usually belong to the "diabète maigre" group, while both forms occur among the older patients.

The relationship between age of onset of diabetes and the use of insulin on Jan. 1, 1956, was studied both for "diabète maigre" and diabète gras." Figures 6 and 7 show that the curve for "diabète maigre" presents an identical pattern for men and women. Here also it is true that diabetes with onset at early age requires more insulin than when it develops at more advanced age. The possibility must, however, be kept in mind that among the patients who developed the disease at early age there may have been several who had been under treatment for a long time, so that they needed more insulin. In patients with onset in adult life, dietary treatment, combined or not combined with moderate quantities of insulin, is often sufficient. In the large majority of "diabète gras" cases dietary treatment is sufficient. As defined before, the diets are calculated to provide minimal glycosuria, to reduce the blood sugar content to values below 200 mg. per 100 ml., and, in the case of overweight diabetic patients, the total caloric allotment is restricted to about 1,200 calories, to produce loss of weight.

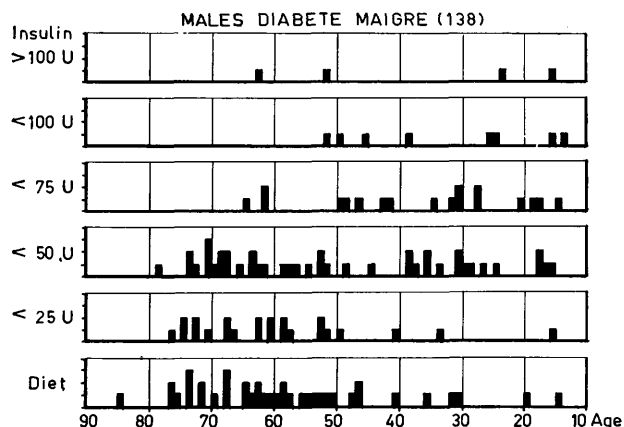


FIGURE 6A

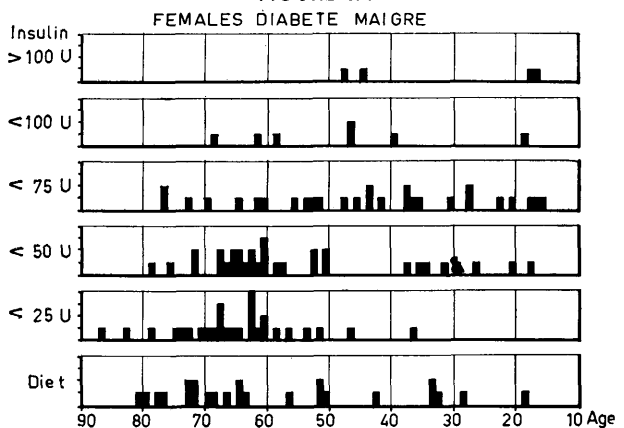


FIGURE 6B

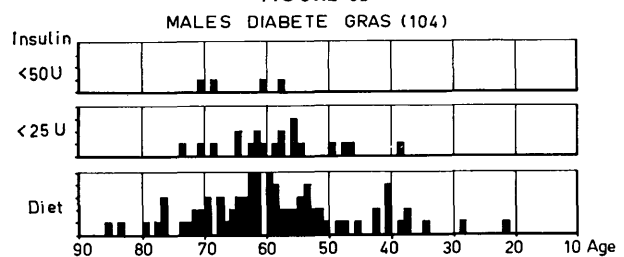


FIGURE 7A

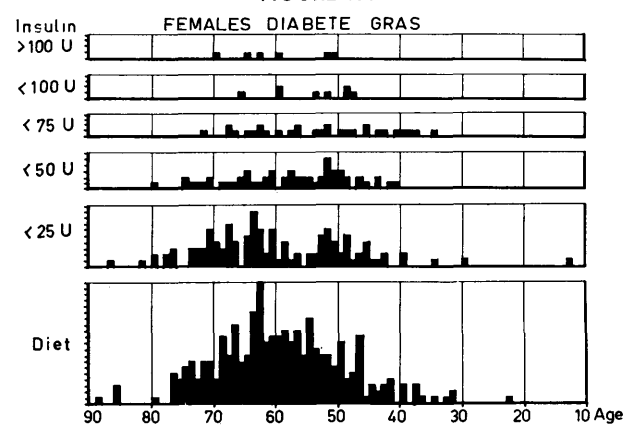


FIGURE 7B

Among the overweight women there were a number who were given higher doses of insulin (> 50 U); such cases are not found among the men. It appeared that twenty of these women did not follow the instruction to restrict the caloric intake and their weight increased. The result of treatment with high doses of insulin in these cases was also poor. The weight of eleven of these patients was reduced but in most cases not to normal values. With high doses of insulin the regulation was satisfactory. In seven cases the weight did not change, and with insulin it was possible to obtain a satisfactory result.

Of 484 women and 100 men with "diabète gras" the body weight was known both at the time of onset of the diabetes and on January 1, 1956. These patients are subdivided into the following four groups, according to the change in weight: Group I: The body weight fell to normal values; Group II: the body weight decreased but is still too high; Group III: the weight has remained the same (i.e., changed less than 1 kg.); Group IV: the weight has increased.

TABLE 3

	Males (100)		Females (484)	
		per cent		per cent
Group I	44	44	122	25
Group II	41	41	217	45
Group III	7	7	47	10
Group IV	8	8	98	20

This table shows that in proportion there was far less loss of weight among women during treatment than among men. From this it is clear that reduction of weight is not only of great importance for the prevention of manifest diabetes, but also that reduction of weight is necessary to reach a balanced carbohydrate metabolism in obese diabetic patients.

SUMMARY

Data of 733 male and 1,379 female diabetic patients have been evaluated. It is shown that female predominance is especially manifest in the fifty years of age and over group.

No relationship was established between the number of pregnancies and pathogenesis of diabetes.

"Diabète maigre" was found in young and older patients; "diabète gras" only at ages over thirty. The in-

cidence of "diabète gras" cases was far higher among women (57 per cent) than among men (22 per cent). Findings among women indicate that obesity is a stimulating factor in the pathogenesis of diabetes mellitus and that the high frequency of diabetes among women over fifty is associated with obesity. The unfavorable influence of obesity on diabetes is indicated by the higher insulin requirement among overweight women, who showed insufficient loss of weight during the treatment.

SUMMARIO IN INTERLINGUA

*Investigationes Statistic In Diabete Mellite*

Es evaluatae datos ab 733 masculos e 1.379 femininas diabeticas. Es monstrate que le predominantia feminin es specialmente manifeste in personas de plus que cinquanta annos de etate.

Esseva establite nulle relation inter le numero de pregnantias del diabeticas e le pathogenese de lor morbo.

*Diabete maigre* esseva trovate in juvene patientes e in patientes de etates plus avantiate. *Diabete gras* occurreva solmente a etates de plus que trenta annos. Le incidentia de *diabete gras* esseva multo plus alte in femininas que in masculos (57 e 22 pro cento, respectivamente). Le datos pertinente al feminas supporta le idea que obesitate es un factor stimulatori in le pathogenese de diabete mellite e que le alte frequentia de diabete mellite in femininas de plus que cinquanta annos de etate es associate con le presentia de obesitate. Le effecto disfavorabile de obesitate super le diabete es reflectite in le plus alte requirimentos de insulina inter femininas con excessos de peso e inadequate perditas de peso sub le effecto del tractamento.

REFERENCES

<sup>1</sup> Spiegelman, M., and Marks, H. H.: Age and sex variations in the prevalence and onset of diabetes mellitus. *Am. J. Pub. Health* 36:26, 1946.  
<sup>2</sup> Pyke, D. A.: Parity and the incidence of diabetes. *Lancet* 1:818, 1956.  
<sup>3</sup> Duncan, G. C.: *Diseases of Metabolism*, 3rd ed., 1952, p. 1106.  
<sup>4</sup> Joslin, E.: *Diabetes Mellitus*, 9th ed., 1952, p. 39.  
<sup>5</sup> Pett, L. B., and Ogilvie, G. F., in Brozek, J.: *Body Measurements and Human Nutrition*, Detroit, 1956, p. 73.  
<sup>6</sup> Bornstein, J.: The insulin content of blood plasma. *Diabetes* 2:23, 1953.