

Aspects of pre-eclamptic toxæmia of pregnancy, consanguinity, and twinning in Ankara

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Summary. It appears that women classed as having pre-eclamptic toxæmia are less frequently consanguineous with their husbands than all other mothers and in particular those mothers classed as having pregnancies complicated by chronic hypertensive disease. Search revealed no evidence for possible biases which could have simulated such findings.

Further evidence is advanced suggesting that, though pre-eclamptic toxæmia is more common in all types of twin pregnancies than in single births, it is more common where the twins are dizygous than where they are monozygous.

It is pointed out that both these findings would be expected if there was a contribution to the aetiology of pre-eclamptic toxæmia by maternal/fetal immunological incompatibility. However, if such a mechanism exists it is not always determined at the same gene locus.

Starting in 1971 a special study was made of all women delivered in the Doğum Evi Hospital, Ankara. From data accumulated after the first 5286 mothers who had been delivered, Stevenson *et al* (1971) concluded that the proportion of women who had pre-eclamptic toxæmia who were related to their husbands was significantly less than in the other patients.

By early 1973, 23 416 mothers with single pregnancies and 271 with twin pregnancies had been studied. Basic information concerning these patients is set out in Table I. Records in respect of 58 of the patients with single pregnancies were incomplete in respect of one or more of the variables presented in subsequent tables, so these forms were ignored and the total in subsequent tables is 23 358. Ten women (none classified as having pre-eclamptic toxæmia) were identified as having been admitted for two pregnancies during the period of the study. The data from both admissions have been included.

TABLE I
OUTLINE OF DATA

Single births	Males Females Total (births)	12 455 10 961 23 416
Twin births	MM pairs MF pairs FF pairs Total (pregnancies) Total (births)	80 112 79 271 542
Grand total (pregnancies)		23 687
Grand total (births)		23 958
Frequency of 'true' pre-eclamptic toxæmia per 1000 total births		2.4
Stillbirth rate per 1000 total births		19.3
Live births—died before leaving hospital per 1000 total births		17.0
'Perinatal' mortality per 1000 total births		36.3
Proportion of mothers in relationship with their husbands:		
Coefficient of inbreeding*	$\frac{1}{16}$ (first cousins)	13.4%
	$\frac{1}{32}$ (first cousins one removed)	2.8%
	$\frac{1}{64}$ or less (second cousins or less)	0.8%
	Any consanguinity	17.0%

* These coefficients are really those of the offspring of such marriages, but as a convenience (with many precedents!) they are applied in this and other Tables to the marriages.

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Methods

Conduct of study. Forms for recording relevant information about patients were bound together in packs of 100. Each pack also had a set of directions for completion of the forms, and a copy of the classification of pre-eclamptic toxæmia (PET) and hypertensive disorders complicating pregnancy, which was that of the American Committee on Maternal Welfare (Hellman and Pritchard, 1971). This classification is, for convenience, reproduced in the Appendix.

Recording of consanguinity. Patients were seen as soon after admission as possible by one of the two social workers and questioned about any relationship with their husbands. If the patient's husband was her first cousin, one of the diagrammatic pedigrees showing the four possible types of first cousin (see Table VIII) was ticked. If there was a relationship, but it was other than that of first cousin, a diagrammatic pedigree was drawn. Coefficients of inbreeding were subsequently added to the records.

For simplicity a single instance of coefficient of inbreeding of 1/8 was classed as 1/16, and two of 1/128 as 1/64. The recording of consanguinity and that of data relevant to PET and its assessment were done independently by different individuals.

In Turkish families, consanguineous marriages are much favoured and relationships of spouses are very important, so that they are well known to, and understood by, spouses. There is little doubt, however, that some marriages classed as non-consanguineous were really between distant relatives.

Recording of toxæmia. The basic data were recorded by the obstetrician in charge of the patient, and the assessment, according to the classification used, was decided upon after discussion with a senior staff member.

The many difficult problems of distinguishing between true PET (however defined and if such an entity exists!) were further complicated in the Doğum Evi

Hospital by the fact that only about 10% of patients were seen at antenatal clinics before the 24th week of pregnancy so that, for most patients, the vital criterion that the blood pressure rose only after the 24th week could not be established. This matter is considered below in comparisons of times when patients with and without PET were first seen (see Table IV). Blood pressures of all patients were taken before discharge from hospital.

Results

Maternal age and parity and frequency of PET by parity. From Table II it will be seen that the mean frequency of pre-eclamptic toxæmia in single pregnancies was 2.4%. A surprisingly high proportion of all women in Ankara are confined in hospital, probably over 95%, and the Doğum Evi, being a large public hospital, admits all who apply. The problems of comparing the frequencies of PET in patients in different hospitals with different admission priorities are well discussed by Davies (1971).

Also from Table II it will be seen that the frequency of PET is relatively high in first pregnancies, falling in subsequent pregnancies, but rising again from fifth pregnancies onwards. This is a very similar pattern to that in the Shatby Hospital, Alexandria (Einen and Topozada, 1966) and in Jerusalem (Davies *et al.*, 1970; Davies, 1971), though the frequencies in both the Doğum Evi and the Shatby Hospitals rise to even higher levels than in Jerusalem in pregnancy orders eight and above.

The data on maternal age and parity in Table II probably give a picture only approximating to the truth, as patients are often uncertain as to their ages, and multipara may not accurately remember previous mature births. Data on abortions in past pregnancies were recorded but showed so many

TABLE II
SINGLE BIRTHS: MATERNAL AGES, MATURE BIRTH ORDERS AND FREQUENCY OF TOXAEMIA BY BIRTH ORDERS

Mature Birth Order*	Maternal Age								True Toxaemia in this Pregnancy	
	0-19	20-24	25-29	30-34	35-39	40-44	45 +	Total	No.	Frequency (%)
1	1557	1878	522	146	35	10	0	4148	112	2.70
2	2149	3762	1308	296	101	21	6	7643	135	1.77
3	454	2177	1259	393	132	15	5	4435	69	1.55
4	123	1009	1011	472	168	21	7	2811	51	1.81
5	19	333	637	513	242	38	6	1788	58	3.24
6	11	174	359	372	209	39	9	1173	45	3.83
7	1	6	9	229	179	50	4	478	23	4.81
8	1	1	8	157	143	41	4	355	14	3.94
9	0	0	1	27	94	27	1	150	9	6.00
10+	0	0	0	7	261	91	18	377	38	10.08
Total	4315	9340	5114	2612	1564	353	60	23 358	554	2.37

* Birth order ignoring pre-28th week miscarriages.

discrepancies as to be worthless. The first column in Table II suggests that a few women have a remarkable number of children before the age of 20 years. The data may not be accurate, but it has to be remembered that in country districts a girl may be married at 12 to 14 years, and Ankara is a magnet for poor labourers from a huge hinterland.

Consanguinity of patients and PET. Table III sets out the numbers of patients with single pregnancies in respect of PET, hypertensive disease complicating pregnancy, and degrees of relationship, if any, to their husbands.

It will be seen that the frequency of any recorded degrees of consanguinity in mothers with PET (IA₁, IA₂, or IB) is 63/554. This is significantly less than the frequency in mothers who had no hypertension or PET (group IV) which was 3873/22 573 ($\chi^2 = 12.4108$, $df = 1$, $P < 0.001$). Consanguinity is also significantly less in mothers with PET than in those judged to have had hypertensive disease complicating pregnancy (IIA₁, IIA₂, IIB) which was 37/188 ($\chi^2 = 7.6133$, $df = 1$, $P < 0.01$).

However, there is no significant difference in the frequency of consanguinity between women who had hypertensive disease (37/188) and those who had neither hypertensive disease nor PET (group IV) (3873/22 573) ($\chi^2 = 0.6663$, $df = 1$, $0.3 < P < 0.5$).

In view of this apparent overall effect of consanguinity, it might be expected that there would be a negative correlation between coefficients of inbreeding and frequency of PET. The frequency of PET in women where the coefficients of inbreeding were 1/16, 1/32, and 1/64, were, respectively 50/3135 (1.59%), 9/669 (1.34%), and 4/178 (2.24%). Unfortunately the numbers in the classes of mothers

with the two lower coefficients of inbreeding are too small to enable any conclusions to be drawn.

In considering Table III the few patients classed as having 'unclassifiable' toxæmia (group III) have been ignored. The classification is vague, and the number very small, so that however they are apportioned to classes I or II would not affect the significance of comparisons.

These data appear to support the suspicions raised by the data from Shatby Hospital, Alexandria (Einen and Topozada, 1966; Stevenson *et al*, 1971) that consanguinity is less frequent in women whose pregnancies were complicated by PET than in other mothers.

There are two possible biases which might effect the data assembled: (1) mothers who subsequently developed PET might, on average, attend antenatal clinics only later in pregnancy than other mothers; (2) consanguinity rates may be falling so rapidly in the growing city of Ankara that it would be expected to be less frequent in younger mothers and in those of low parity than in older multiparous women. Further, it is these younger women who account for most cases of PET.

Table IV does not suggest that bias arises from differences in proportions of mothers first seen in varying stages of pregnancy. Evidence for the second possible source of bias is not apparent from the data in Tables V and VI. There is no evidence of significant differences in frequency of consanguinity in younger compared with older mothers, or those in early birth orders compared with later birth orders.

Another possible source of bias would be if both PET and consanguinity were more common in mothers from poorer homes than in those more

TABLE III

SINGLE PREGNANCIES: TOXAEMIA OF PREGNANCY, HYPERTENSIVE DISEASE OR NEITHER, AND CONSANGUINITY OF MOTHERS AND THEIR HUSBANDS

Classification of Mothers by Presence or Absence of Toxaemia or Chronic Hypertensive Disease*	Relationships of Mothers and their Husbands (coefficient of inbreeding)				Totals	
	1/16	1/32	1/64	Zero	No.	Consanguinity (%)
<i>Group I: Pre-eclamptic toxæmia</i>						
IA ₁ (mild)	38	9	1	364	412	11.65
IA ₂ (severe)	8	0	1	100	109	8.25
IB (eclampsia)	4	0	2	27	35	18.18
Total toxæmia	50	9	4	491	554	11.37
<i>Group II: Hypertensive disease</i>						
IIA ₁ : Known before pregnancy	3	0	1	16	20	20.00
IIA ₂ : Discovered during pregnancy	26	4	3	135	168	19.64
IIB: With superimposed toxæmia	0	0	0	0	0	—
Total hypertensive disease	29	4	4	151	188	19.68
<i>Group III: Unclassifiable 'toxæmia'</i>	7	2	0	34	43	20.93
<i>Group IV: No hypertension or toxæmia</i>	3049	654	170	18 700	22 573	17.16
All mothers	3135	669	178	19 376	23 358	17.05

* For classification see Appendix.

TABLE IV

SINGLE PREGNANCIES: TIMES WHEN FIRST SEEN IN PREGNANCY IN WOMEN WHO DID OR DID NOT HAVE PRE-ECLAMPTIC TOXAEMIA

Weeks when First Seen	Pregnancy		
	Pre-eclamptic Toxaemia (IA ₁ , IA ₂ , and IB)	No Pre-eclamptic Toxaemia (II, III, and IV)	Total
0-11	25	1051	1076 985 396 1216 539 19 146
12-17	24	961	
18-23	13	383	
24-29	25	1191	
30-35	14	525	
36 +	453	18 693	
Total	554	22 804	23 358

favoured socially and economically. After much discussion it was decided not to attempt to ask questions of mothers which might have permitted some socioeconomic groupings. In a trial before recording began it was found that many women said they did not know their husbands' occupations, and other questions about income aroused resentment and suspicion. Patients admitted to the hospitals are predominantly from low income households, the majority of husbands being casual workers, or at least not members of any social security scheme. Others were small street traders. Very few were artisans or could be classed as skilled or semiskilled workers.

TABLE V

SINGLE BIRTHS: PRE-ECLAMPTIC TOXAEMIA IN WOMEN CONSANGUINEOUS AND NOT CONSANGUINEOUS WITH THEIR HUSBANDS, RELATED TO MATERNAL AGE

Classification of Toxaemia*	Maternal Age								
	0-24			25 +			Total		
	Con-sanguinity	No Con-sanguinity	Total	Con-sanguinity	No Con-sanguinity	Total	Con-sanguinity	No Con-sanguinity	Total
PET (I)	35 (10.90%)	286	321	28 (12.0%)	205	233	63 (11.4%)	491	554
No PET (II, III, and IV)	2266 (17.0%)	11 068	13 334	1653 (17.5%)	7817	9470	3919 (17.2%)	18 885	22 804
Total	2301 (16.8%)	11 354	13 655	1681 (17.3%)	8022	9703	3982 (17.0%)	19 376	23 358

* See Appendix.

TABLE VI

SINGLE BIRTHS: PRE-ECLAMPTIC TOXAEMIA IN WOMEN CONSANGUINEOUS AND NOT CONSANGUINEOUS WITH THEIR HUSBANDS, RELATED TO BIRTH ORDER

Classification of Toxaemia	Birth Order						All		
	1-4			5 +					
	Con-sanguinity	No Con-sanguinity	Total	Con-sanguinity	No Con-sanguinity	Total	Con-sanguinity	No Con-sanguinity	Total
PET (I)	44 (12.0%)	323	367	19 (10.2%)	168	187	63 (11.4%)	491	554
No PET (II, III, and IV)	3174 (17.0%)	15 496	18 670	745 (17.3%)	3389	4134	3919 (17.2%)	18 885	22 804
All	3218 (16.9%)	15 819	19 037	764 (17.6%)	3557	4321	3982 (17.05%)	19 376	23 358

TABLE VII

SINGLE PREGNANCIES—TOXAEMIA OF PREGNANCY AND HYPERTENSION BY TYPE OF FIRST-COUSIN MARRIAGE

Type	First Cousin Type*				Total
	1	2	3	4	
True toxæmia	16	10	10	14	50
Hypertension (or unclassifiable)	12	8	7	9	36
Neither	1007	671	640	731	3049
Total	1035	689	657	754	3135
Frequency of true toxæmia	1.54%	1.45%	1.53%	1.86%	1.59%

* See Table VIII.

Types of first-cousin marriages and PET. Table VII sets out the data for first-cousin marriages broken down by type on PET. There is no suggestion that any one type of first-cousin marriage is more relevant to PET than another.

Types of first-cousin marriages in Alexandria and Ankara. In Alexandria the frequency

of first-cousin marriages in 9586 mothers was 22.0%, which is higher than in Ankara (13.4%). However the distribution of the types of first-cousin marriages was very different in the two hospitals as can be seen from Table VIII.

In Ankara about one-third of all first-cousin marriages are of type 1, between the children of two brothers. However, in Alexandria the most frequent type is 3, where a man marries his father's sister's daughter.

It is interesting to note that in neither country, at least among professional people, does there seem to be any recognition of these preferences. When pointed out no consistent explanations are offered in either country. (The problem is of interest to the social anthropologist.)

PET and twin pregnancies. In the preliminary paper (Stevenson *et al*, 1971), analysis of twin data available from Alexandria, the British National Birthday Trust, Belfast, and Oxford showed that PET was consistently lower in mothers

TABLE VIII

SINGLE BIRTHS: TYPES OF FIRST-COUSIN MARRIAGES, ANKARA AND ALEXANDRIA

Types of First-cousin Marriage	Numbers and Proportions of each Type	
	Ankara	Alexandria
1. Spouses were offspring of two brothers	1035 (33.0%)	506 (27%)
2. Spouses were offspring of two sisters	689 (22.0%)	415 (22%)
3. Woman was married to son of her mother's brother	657 (21.0%)	566 (30%)
4. Woman was married to son of her father's sister	754 (24.0%)	405 (21%)
Total first-cousin marriages	3135	1892

TABLE IX

FREQUENCIES OF PET IN PREGNANCIES BY TWIN TYPES

Centre	Like Sexed Pairs		Unlike Sexed Pairs		Estimated			
	All	PET	All	PET	Monozygous Pairs		Dizygous Pairs	
					All	PET	All	PET
Alexandria	204	24 (11.8%)	143	21 (14.7%)	61	3 (4.9%)	286	42 (14.7%)
UK (National Birthday Trust)	142	54 (38.0%)	54	28 (51.9%)	88	26 (29.5%)	108	56 (51.9%)
Belfast	337	59 (17.5%)	208	53 (25.5%)	129	6 (4.6%)	416	106 (25.5%)
Oxford	314	128 (40.8%)	185	93 (50.3%)	129	35 (27.2%)	370	186 (50.3%)
Ankara	159	14 (8.80%)	112	13 (11.6%)	47	1 (2.1%)	224	26 (11.6%)

TABLE X

SINGLE BIRTHS: CONSANGUINITY AND PERINATAL DEATHS

Coefficient of Inbreeding	Outcome of Pregnancy							Per 1000 Total Births	
	MLB	FLB	MLB (D)	FLB (D)	MSB	FSB	Total	Stillbirth Rate	'Perinatal' Mortality
1/16: type 1	557	437	9	11	12	9	1035	20.3	39.6
type 2	322	329	6	7	11	14	689	36.3	57.8
type 3	331	299	9	4	7	7	657	21.3	41.1
type 4	373	356	7	2	8	8	754	21.2	33.2
total	1583	1421	31	24	38	38	3135	24.2	41.8
1/32	316	322	9	6	11	5	669	23.9	46.3
1/64	97	70	2	4	2	3	178	28.1	61.8
All consanguineous	1996	1813	42	34	51	46	3982	24.4	43.4
Zero	9851	8849	175	148	178	175	19 376	18.2	34.9
Total births	11 847	10 662	217	182	229	221	23 358	19.3	36.3

with pregnancies of like sexed than in those with unlike sexed twins and that estimates suggested highly significantly higher rates in mothers with dizygous than with monozygous twins. When this paper was published there were insufficient data to analyse from Ankara, but information on 271 pairs has now accumulated, and as can be seen from Table IX, shows the same order of magnitude of higher frequency of toxæmia in mothers with unlike sex twin pregnancies as in the other studies. However, the numbers from Ankara are small and the estimated difference between monozygous and dizygous twins is not technically significant, $\chi^2 = 2.9066$ (Yates correction) $P < 0.1$. Nevertheless, the consistency of the five sets of data on toxæmia in twin pregnancies is very impressive.

Consanguinity and perinatal death. It has been reported from time to time that stillbirth rates and perinatal mortality are higher in the progeny of related than of unrelated parents (Stevenson *et al*, 1966). The relevant data from this study are set out in Table X. It will be seen that the 'perinatal' mortality in offspring of mothers in any way related to their husbands (173/3982) is significantly higher than in those of unrelated mothers (676/19 376): $\chi^2 = 6.6630$, $df = 1$, $P < 0.01$. 'Perinatal' mortality is used in the loose sense of stillbirths plus deaths of infants in hospital per 1000 total births.

Discussion

It is not intended to discuss the numerous hypotheses as to the aetiology of toxæmia. Excellent reviews are those of Jeffcoate (1966) and of Davies (1971) who both quote Zweifel's dictum (1895) that pre-eclamptic toxæmia is the 'disease of theories'.

It has often been suggested that a factor in the aetiology could be a maternal/fetal incompatibility and in the most general terms it is clearly more likely that women and their husbands who are consanguineous will on average have more identical ancestral genes in common than will spouses who are not related. A conceptus of such a marriage would in turn be less likely to have genes not possessed by their mothers and possibly producing foreign antigens. Studies of consanguinity and PET are not practicable unless, in the population sampled, the consanguinity rate is relatively high. For example, in the United Kingdom, where the frequency of consanguineous marriages is perhaps about 1/300, and of PET perhaps 3/100, the random chance of PET in a consanguineous marriage is 3/20 000, so that studies would be impossibly laborious if sufficient data were to be obtained. On

the other hand consanguinity is now only high in certain relatively underdeveloped countries. It is, therefore, difficult to find places in which there exist the necessary conditions for a study which can be undertaken successfully in a few years. These conditions are: hospitals where the clinical standards are high, where there are a large number of births each year, and where the frequency of consanguineous marriages is high. In the Doğum Evi Hospital all three conditions are satisfied (the responsibility for suggesting the first is that of A.C.S.)!

The biggest problem in all studies of PET is in distinguishing between PET however defined, and a manifestation during pregnancy of pre-existing essential hypertension or chronic kidney disease. In this study the fact that so few patients were seen before 29 weeks makes the problem even more difficult.

However, at least approximately the same proportions of women who do and who do not develop PET are seen before 24 weeks (Table IV).

The data in Table III seem to suggest strongly that consanguinity is less frequent in women classed as having PET than in others. It is interesting to note that the criterion of consanguinity identifies as different those women classed as having PET (group I) and those classed as having chronic hypertensive disease (group II).

Browne and Sheumack (1956) produced evidence that hypertensive disease was more common in close relatives of patients regarded as having PET than in others. However, chronic hypertensive disease would be unlikely to be more common in women who contracted consanguineous marriages. The genetic contribution to familial hypertensive disease is probably multigenic (Hamilton *et al*, 1954) and might, under certain circumstances, be more common in women whose parents were consanguineous.

As discussed in the earlier paper, two 'models' of maternal/fetal incompatibility based on a single gene locus as a possible explanation of PET have been advanced and considered in association with data on familial occurrence of PET. If the alternative alleles are T and t, then on the first model the prerequisites for incompatibility are Tt fetus in a tt mother (i.e., a rhesus-like situation), and the second a tt fetus in a Tt mother. It is easy to produce elaborate expressions based on either of these models for prediction of frequencies in specified relatives in women related to their husbands, and in monozygous and dizygous twin pregnancies, assuming various gene frequencies. However, both these hypotheses involving a single locus are incompatible with the

phenomenon of a woman having a pregnancy complicated by PET which results in a daughter who, in turn has a pregnancy complicated by PET. Yet there can be no doubt that this occurs (Humphries, 1960; Chesley, Annitto, and Cosgrove, 1968). However, PET in a daughter born from a PET-complicated pregnancy of her mother is perfectly compatible with series of alleles at different loci each capable of determining the incompatibilities in mother and daughter.

The data on twin pregnancies are also explicable on a maternal/fetal incompatibility hypothesis whether determined at one or several gene loci. As is clear from Table IX, PET frequencies in pregnancies with like sexed twins are lower than in those with twins of unlike sex, but the differences are of borderline significance. However, when estimates were made from the data of the frequencies in monozygous and in dizygous twins, though these estimates were not necessarily very accurate, the significances of the differences are impressive; even if the higher frequency of PET in the presumptive dizygous twin pregnancies is not technically significant in the present data.

It seems, therefore, that the evidence in accord with a hypothesis of fetal incompatibility contribution to PET is impressive both from study of consanguineous marriages and twin pregnancies. That is not to say that if there is such a contribution it is the only factor, or even the factor which contributes most to the frequency of PET. It could, however, be the *sine qua non* of the occurrence of PET with endocrine, nutritional, and other less clearly identified factors determining sufficient disturbance in many patients for the clinical signs to reach the, of necessity, arbitrary criteria which are accepted for a clinical diagnosis.

There are two conclusions which seem important to the authors: (1) within a few years there will be few communities in the world where consanguinity rates will be sufficiently high for our findings to be confirmed in another population. It is to be hoped that appropriate work will be done. (2) The authors do not feel competent to discuss work which has been done on immunological responses by mothers to genetically 'foreign' fetuses, but there are many

indications that such responses occur in pregnancy (Payne and Rolfs, 1958; Hulka *et al*, 1963; Currie and Bagshawe, 1967; Van Rood, Eernisse, and Van Leeuwen, 1968; Loke, Joysey, and Borland, 1971).

What do not appear to have been published are accounts of work on such responses specifically in women where pregnancies were complicated by pre-eclamptic toxæmia. Again, it is to be hoped that *ad hoc* studies will be undertaken.

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Appendix

CLASSIFICATION

(I) Acute toxæmia

IA₁ = acute toxæmia (onset after 24 weeks) pre-eclamptic/mild:

- (1) Blood pressure after 24 weeks 140 mm Hg or more (systolic) or a rise of 30 mm or more above usual level, (diastolic) 90 mm or more or a rise of 15 mm or more above usual level.
- (2) Proteinuria of significant degree.
- (3) Persistent oedema of the hands or face.

IA₂ = acute toxæmia (onset after 24 weeks) pre-eclamptic/severe:

- (1) Blood-pressure 160 mm Hg or more (systolic) or 110 mm or more (diastolic) on at least two occasions at intervals of 6 h with patient at bed rest.
- (2) Proteinuria 5 g or more (+ + + or + + + +).
- (3) Oliguria (400 ml or less in 24 hours).
- (4) Cerebral or visual disturbances.
- (5) Pulmonary oedema or cyanosis.

IB = Eclampsia (convulsions and/or coma when associated with hypertension, proteinuria, oedema).

(II) Chronic hypertensive (vascular) disease associated with pregnancy

IIA = Without superimposed acute toxæmia (no exacerbation of hypertension or development of toxæmia).

IIA₁ = Hypertension known to have antedated pregnancy.

IIA₂ = Hypertension discovered in pregnancy (before 24th week) and with post-partum persistence.

IIB = With superimposed toxæmia.

III = Unclassified toxæmia (data insufficient to differentiate the diagnosis).

None = No toxæmia.