

PLACENTAL INFARCTION.

In its Relation to the Toxaemias of Pregnancy.

A Thesis

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of

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by

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INTRODUCTION.The Subject.

This Thesis is intended as a short treatise on the work I have done recently on investigation of placental infarction.

The Object.

The objects of the investigation were to discover Firstly, Does placental infarction cause pregnancy toxæmia? if so Secondly, How much of the placenta could be "infarcted" before the patient would show clinical signs or symptoms of toxæmia?

The Materials.

The materials were, one thousand placentae from consecutive deliveries in the normal labour wards.

The Time and Place.

The work was undertaken during the Autumn and Winter of 1947, and Spring of 1948 in the Simpson Memorial Maternity Pavilion, Royal Infirmary of Edinburgh. It was undertaken by kind permission of Professor R. J. Kellar, to whom I am deeply indebted for patient counsel and encouragement.

The microscopic examinations and the photographic work were done in the laboratory of Professor Kellar's department at the University of Edinburgh.

PLACENTAL INFARCTION.

In its relation to the toxæmias of pregnancy.

Historical Survey.

A great deal of effort has been expended and much research work has been done in attempts to elucidate the cause of the toxæmias of pregnancy.

Numerous investigators have propounded a relationship between Maternal toxæmia and infarction of the placenta.

As far back as 1668 Mauriceau called attention to certain white areas in the placenta, these he called "Schirrus" of the placenta, he did not advance any theories as to the nature or cause of these white areas.

Cruveilhier about the same time called them "Atrophy", but at a later date he suggested the name "Placental Apoplexy", he was then supported by Jacquemier, Gierse, Meckel and others.

Workers like Bracket, Wilde, Simpson, Hegar, and others believing these lesions to be of inflammatory origin called them "Placentitis".

Zilles thought that these lesions were Syphilitic and called them "Gummata", while Simpson at that time, 1845, thought them to be of tuberculous origin and called them "Phthisis of the placenta". Rohr, Martin, and Delore thought that the lesions were due to some form of thrombosis.

Eden in 1897 stated that by subendothelial thickening in the foetal vessels a gradual but characteristic endarteritis is produced, vessel lumina are/

are then obliterated, and by a continuation of that process, or by a loss of endothelium there is consequent thrombosis.

Montgomery in an article written in 1931 describes the change in the tissue of these lesions as a localised degeneration of the villous syncytium with a superimposed process resembling thrombosis.

Apparently Ollivier in 1840 was the first to call these lesions in the placenta "Infarcts".

Many investigators later gave their support to this theory, and the name "Placental Infarct" is in common use today.

What is meant by infarction?

MacCallum, after describing slighter degrees of Anaemia, says, "More complete anaemia commonly causes death of the affected part, and this is the important feature in the production of infarction.... The cells lose the aspect which they possessed during life, they are dead cells, entangled and held in a coagulum which involves the whole area of the tissues."

MacCallum goes on to show that he believes the essential cause of infarction to be blockage of a nutritive blood supply to a certain area, notably blockage of an artery. This, in turn, involves the destruction of a whole area of specialised tissue at one time, and usually gives rise to certain reactive changes, while the tissue destroyed undergoes simultaneous death.

Young, 1914, advanced the theory that the nourishment/

nourishment of the chorionic villi was wholly from the maternal circulation.

He points out that in the early development of the placenta, when the villi are not themselves vascularised at all, growth is very rapid. The villi of Hydatidiform Mole grow rapidly yet the gelatinous stroma is not vascularised. Fragments of undegenerated syncytium have been found in other organs of pregnant women, and in such a situation the only possible source of nourishment is maternal.

In ectopic pregnancy also, fragments of undegenerated syncytium may be found growing, yet detached from the ovum.

In a syphilitic placenta, the villi are avascular or very poorly vascularised; here one supposes that the villi must necessarily be nourished by the maternal blood. (Browne finds this the most convincing factor in proof of the maternal hypothesis.)

Clements in 1934 writes, "It is generally conceded that an infarct is an area of coagulation necrosis resulting from the arrest of circulation in an artery supplying the part. Thus the obstruction of an end-artery in an organ such as the liver, kidney, or spleen results in starvation of that part whose nutrition was supplied by the occluded vessel, causing death of the tissue with a more or less characteristic infarct formation."

It is the opinion of many observers that the pathological process involved in placental infarction, however, /

however, is of an entirely different nature.

The circulation in the human placenta entails two separate and distinct systems, foetal and maternal, with no direct communication between them. "The interchange of metabolic products occurs through the biochemical processes of Osmosis and diffusion. It has been quite conclusively established that the chorionic villi depend on maternal blood for their nourishment and growth. Pathological changes in the villous vessels, therefore, does not account for placental necrosis."

Recent research has shown that the decidual arteries discharge their blood into a subchorioidal space which communicates freely between the villous stems. The blood is then collected by the decidual veins. The villi are thus bathed in a pool of maternal blood, rather than by any individual blood vessel, so that it appears unlikely that interference with the circulation in one or more decidual arteries can affect placental nourishment.

A possible exception to this, as has been pointed out by many observers, is marginal infarction due to deficiency of blood supply at the edge of the placenta.

This is further substantiated by rentgenological studies of Thoms, 1926, showing that especially in the later months of pregnancy the maternal circulation appears insufficient to nourish the chorionic villi at the edge of the placenta.

Hellman, 1947, in "Gynaecological and Obstetrical Pathology", by Novak (2nd Edition), says, "To understand the/
the/

"the significance of the degeneration of any organ its source of nutrition must be clear. At the present time this is not definitely known as regards the placenta; however, evidence has slowly accumulated which is predominantly in favour of maternal and not foetal nutrition of the organ." Young, Strachan, Siddall, and Stander have all supported this concept, while Eden, Williams, and Ackermann are of opinion that the nutrition of the placenta is through the chorionic vessels. Hellman continues:-

1. "In the first place, foetal death does not cause placental death, but merely a disuse endarteritis of the villous vessels.

2. "Secondly, the placenta can be present and alive without a foetus, as in the case of pathological ova, where only placenta and membranes are present, i.e. Hydatid Mole.

3. "Thirdly, the villi grow prior to the formation of chorionic vessels, and during the period when these vessels do not form a continuous system as shown in Kertig's excellent paper on Angiogenesis of the placenta.

4. "Fourthly, the results of animal experiments show that the foetus is not necessary for growth or full term delivery of the placenta, since when the foetus is removed in the last months of pregnancy the placenta continues to develop in situ until the usual duration of term, when it is expelled. This was first demonstrated by Newton for the mouse, and later confirmed by Kirsch in the rat, and Van Wagenen in the monkey."

Almost/

Almost the same arguments as Young used so many years ago in favour of the maternal source of nourishment of the placenta.

A short review of some of the literature.Pathology of Infarcts.

The pathology of infarcts has been described and discussed by very many investigators and writers. Eden, Williams, Young, Strachan, McNalley described them with but slight differences in classification. Siddall and Hartman classified infarcts in four types.

I. Type I. Fully defined pearl grey formations occurring in the depth of the placenta, but also at the surface and margins. They consist of fibrin and villi, extension is by peripheral involvement of villi.

II. Type II. Sharply demarcated areas varying from a few m.m. to several c.m. in size, red, brown, or brick coloured consisting of bloodclot and fibrin.

III. Type III. Similar to type II except that they are paler and contain more fibrin.

IV. Type IV. Round, oval, or pyramidal bodies varying from a few m.m. to several c.m. in size, dark brown, yellow or white consisting of closely packed villi with widely distended vessels all cemented together with a thin layer of fibrin.

The descriptions of infarcts in their studies by Bartholomew and Kracke correspond very closely to that of Siddall and Hartman.

Susanne Paterson in 1923 examined 200 consecutive placentae. She described three distinct types of placental infarcts.

I. Type I. Mural Thrombosis; in this type she believed that fibrin was laid down over damaged syncytial/

syncytial cells, and so formed by gradual growth the common white fibrin infarct.

The common marginal infarct was in every instance composed of fibrin.

11. Type 11. The true infarct. These appear in general under the decidua and are true infarcts, they are dark red or light red in colour and generally gradually become pale, the cause is a separation of the placenta by a haematoma or by the formation of an intraplacental haematoma.

Practically all observers agree that there is an intense congestion of the villi with what virtually amounts to an obliteration of the maternal blood space. This is followed, as in other infarcts in other organs, by a slow necrobiosis.

111. Type 111. Haematomata. These are pink or white or laminated, they consist of blood clot and thrombosed villi.

Hellman in Novak's "Gynaecological and Obstetrical Pathology" 1947, (2nd Edition), describing these lesions uses different terminology.

1. Type 1. Generally known as subchorionic infarction, he calls subchorionic deposition of fibrin, and goes on to say that it is seen in nearly every placenta after the sixth month. This was borne out in my present survey.

11. Type 11. A. Ischaemic necrosis of villi due to fibrin deposition. The deposition of fibrin is initiated by degenerative changes in the syncytial layer/

layer on its internal and external surfaces. Hellman continues, "The syncytium is analogous to the endothelial lining of blood vessels; with the destruction of this lining the power of the vessel, or, in the case of the placenta the power of the boundary of the intervillous spaces to prevent coagulation is destroyed." The villus may become encased in fibrin to such an extent that it is excluded from its source of nourishment, the maternal circulation, a true placental infarct is then formed.

Type 11. B. The second thing that may happen is the formation of a large area of fibrin in the intervillous space; this Hellman calls "Intervillous deposition of fibrin".

111. Type 111. "Intervillous Thrombosis". This is due to the sudden coagulation of blood in the intervillous space. Hellman adds two subgroups.

A. "Ischaemic Necrosis of villi" due to interference with the maternal circulation before it gets to the placenta. This is the kind of lesion that Williams called an atypical white infarct. Microscopically the villi are closely packed and frequently adherent.

B. Ischaemic Necrosis of Villi mixed type. At the margin of nearly every placenta are firm, yellow-white, dry, coarsely granular areas extending into the placenta for varying distances. They are roughly triangular on gross section, and on microscopical section show a combination of necrosis of villi due to fibrin/

fibrin deposition and necrosis of villi due to interference with the maternal circulation. R. A. Bartholomew, 1947, reviews a case of "Thrombosis of the Placental Veins". "A thrombosed vein was seen on the foetal surface extending centrally to the cord, a broad area of acute infarction was present where the vein emerged from the foetal surface of the placenta and was plainly demarcated from the uninvolved portion of the placenta. The consistent association of acute and subacute infarction of the placenta with toxæmia of pregnancy, and the absence of these lesions in placentae from normal pregnancies have been confirmed by Paterson, Hunt and Nicodemus, and more recently by Falkiner.

"Still more recently Hill and Trimble failed to confirm these findings."

My present studies also fail to confirm these findings.

Pre-eclamptic toxæmia and Eclampsia.

Pre-eclamptic toxæmia has been defined as "A condition occurring in pregnant women characterised chiefly by a rise in blood pressure, oedema, and albumin in the urine, and often ending in convulsions."

There are many theories about the aetiology of pre-eclamptic toxæmia and eclampsia, but none are entirely satisfactory.

1. "The Intestinal Toxin Theory", advanced by Tweedy in 1913.

The main argument of this theory is that the "Antibodies" were insufficient to neutralise the added products of placental and foetal metabolism, so protein poisoning resulted. On this the treatment known as "low protein diet" is based.

11. "The Placental Theory" advanced by Young in 1914.

The main argument in this is that, from the "infarcted" placental tissue, toxic substances of great potency are absorbed into the maternal blood. He emphasises the fact that it is the recent autolytic changes in the infarcted tissue that generate the poison.

111. "The Water Poisoning Theory" advanced by Zangemeister in 1915.

He believed that there was increased retention of water in the body due to some toxin acting on the permeability of the capillaries.

The oedema of brain cells leading to increased intracranial/

intracranial pressure, resulting in irritability and convulsions, also in swelling of kidney tissue, etc. He does not explain the origin of the toxin.

1V. "The Dietetic Deficiency Theory" of Theobald in 1930.

A diet apparently adequate for the mother is not adequate for mother and foetus. He believes that deficiency of different vitamins and minerals all play a part.

He states that disturbance of the Calcium metabolism is the most important single factor involved.

The serum calcium may be normal, and the deficiency is probably in the ionised calcium only.

Other authors support the theory of lack of vitamins A. B. C. D., especially B.1. (Thiamin).

V. "The Endocrine Theory."

Of late years a great deal of attention has been focussed on the endocrine system, as a cause of the toxæmias of late pregnancy.

Hoffmann and Anselmino, 1931, claimed that the posterior pituitary contains two secretions concerned in the production of eclampsia. First, an antidiuretic factor which causes oedema, and second, a blood pressure raising substance. They claim that both of these could be demonstrated experimentally.

Other workers failed to confirm this.

Cushing in 1934 described an infiltration of the posterior pituitary by basophil cells from the anterior lobe, in hypertension and eclampsia. He believed this was the cause.

Biggart/

Biggart, in 1935, after examination of 1000 human hypophyses, found that marked basophil infiltration may be found in the absence of either hypertension or eclampsia.

Smith and Smith in 1935 claimed that "imbalance" between oestrin, pregnandiol, and prolan, may be an important factor in the onset of toxæmia.

Taylor and Scadron in 1940, however, found that the serum prolan in eclampsia was within normal limits.

Smith and Smith, 1948, (British Medical Journal, Jan. 1948), in an article entitled "Menstrual Toxin", state that they have demonstrated that "the menstrual discharge contains an atypical euglobulin derived from the endometrium during the last stages of its regression. It is a tissue damaging agent which acts apparently by virtue of its vaso-constrictive properties. It is also fibrinolytic, and immunological studies have identified it with "necrosin", a toxic factor found by Menkin in inflammatory pleural exudate in dogs. Moreover the pseudo-globulin fractions of this exudate and of menstrual discharge will neutralize the effects of the toxic euglobulin fractions."

Smith and Smith point out that the identification of a product of endometrial breakdown with a protein released by cellular injury may indicate that tissue katabolism from various causes may release such a toxin. This, they say, in turn, suggests a common pathogenesis for such conditions as traumatic shock, the crush syndrome, the toxæmias following burns, and possibly also the toxæmias of pregnancy, particularly concealed/

concealed accidental haemorrhage.

They continue, "The toxæmias of pregnancy are involved in this theory, because further research has revealed that there is present in the blood of menstruating women, of women in labour, and of women with pregnancy toxæmia a euglobulin fraction with fibrolytic activity and a pseudo-globulin fraction with a counteraction. These properties are absent from the blood of women during normal pregnancy and in the intervals between periods."

Smith and Smith suggest that in menstruation, labour and toxæmia, these substances result from tissue breakdown consequent on the withdrawal of hormonal support.

Smith and Smith further point out that the finding of a fibrinolysin and of a protective pseudo-globulin in the blood in pregnancy toxæmia serves as a reminder that menstruation and toxæmia present other similarities, such as a tendency to water retention, a withdrawal of oestrogen and progesterone, and clinical improvement when the uterus empties itself of its contents.

They contend that menstrual toxin is the precipitating cause of toxæmia, and they are making clinical trials to determine the value of protective pseudo-globulins in the treatment of pre-eclampsia.

There have been many other theories, but the cause of eclampsia is still unknown.

J. H. Hill and W. K. Trimble in 1945 tell of 640 placentae from consecutive deliveries fixed in 10%

Formaldehyde/

Formaldehyde solution for four to six weeks, then examined grossly for infarcts involving necrosis of villi. 42 of these placentae were from patients with a definite picture of toxæmia. Only eight of these had infarcts extensive enough to distinguish them from placentae of non-toxic patients. Of the 598 placentae from patients with normal pregnancies, 13 showed infarcts similar to the 8 from patients with toxæmia.

Bartholomew has offered some evidence showing that the hypercholesterolaemia found in pre-eclamptic toxæmia may be accompanied by placental infarction. He argues that its genesis is in the weakened condition of the placental arteries due to the high cholesterol.

The evidence offered by Hill and Trimble and by Bartholomew does not support the contention of James Young who declares that the autolyzed products from placental infarction causes pre-eclamptic toxæmia.

Eardly Holland, while admitting that infarcts are more frequent in albuminuria and eclampsia, says that "they may be looked upon as the result of a chronic toxæmia; as to their connection with eclampsia, they are merely accompaniments and not consequences."

The presence of these degenerative changes in eclamptic placentae has been investigated by Brindeau and Nattan-LARRIER who gave them no special significance.

Hypertension.

Hypertension has long been associated with placental infarction and pregnancy toxæmia.

The literature on hypertension in pregnancy is vast. I shall only quote from a few of the more recent writers.

In a series of 239 pregnancies in patients with hypertension in 1942, F. J. Browne and Gladys Dodds found some exacerbation of rise in blood pressure alone in 61%, and added signs of albuminuria, oedema, antepartum haemorrhage (6 cases), eclampsia (2 cases), and serious changes in the fundus oculii (6 cases). In 17% of the cases no exacerbation in any form took place. "The immediate maternal mortality is low; of 222 cases only 2 patients died, one of congestive heart failure, the other of bilateral cortical necrosis of the kidneys. The outlook for the foetus is not unfavourable. In this series of 293 pregnancies the foetal and neonatal mortality rate was 16.2%." They say that in a twelve year follow up "we observed 65 patients in 86 pregnancies. Pregnancy did not seem to have any ill effects in 52 of the 65 patients. In seven the condition was unknown before pregnancy, and six are dead." They continue, "In spite of the six fatal cases, we believe that the large majority of patients with simple hypertension may pass even through several pregnancies, go to term and give birth to live children without suffering any demonstratable deterioration in their condition."

F. J. Browne in 1946 writes, "Hypertension is one of/

of the earliest and most constant signs of pre-eclamptic toxæmia, yet its cause remains undetermined."

The investigations of Kellar and Sutherland have shown that it is due not to a nervous mechanism but to a humoral substance. It is not known what this humoral substance is but it has been demonstrated that it is not Renin, Hypertensin, Adrenalin, or Tyramine.

Hoffmann and Anselmino and Kennedy claimed that in pre-eclamptic toxæmia and eclampsia there was in the patient's circulation excess of a pressor substance derived from the posterior pituitary gland.

This pressor principle was demonstrable in excess in ultra filtrates of the plasma of all pre-eclamptic or eclamptic patients whose blood pressure exceeded 180 mm.Hg.

Other workers failed to confirm these claims.

Byrom, in 1938, discussing the question as to whether the excess of a pressure substance can be the cause of hypertension, says, "The amount of vasopressin required to produce it would be so large that it is difficult to believe that eclampsia can be due wholly to over-secretion of this hormone. The question therefore arises whether some dislocation of the equilibrium arising out of pregnancy may not render the vessels over sensitive to this hormone."

Bourne and Burn claimed to have found that the response of uterine muscle to oxytocin could be greatly enhanced by Oestradiol Benzoate. This suggested to Byrom the study of the effect of sex hormones on the response of the rat to vasopressin. He concluded that gonadotrophic/

gonadotrophic hormone though predominantly luteinizing in action, caused sensitization by stimulating ovarian secretion of oestrin, and that oestrin sensitization is in some way concerned in the genesis of eclampsia.

Shockaert and Lambillon, using Tonephin, and simultaneously and independently Dieckmann and Michel, using pituitrin, showed that nulliparous women, normal pregnant women, and women suffering from pre-eclamptic toxæmia, reacted differently to injected pressor substances. This work was confirmed in its essentials by De Valera and Kellar, and by Browne.

Smith and Smith, in 1935, using Synapoidin (a synergistic preparation containing Anterior Pituitary extract in combination with urinary chorionic gonadotropin) came to the conclusion that not Oestrin but gonadotropic hormone is the sensitizing substance.

F. J. Browne in summing up his work on the subject in 1946 says, "Evidence is brought forward that the cause of hypertension in pre-eclamptic toxæmia is an abnormally increased sensitivity of the vascular system to pressor hormones rather than the presence in excess of the pressor hormone itself.

"It is proved that this abnormal sensitivity is not inherent or constitutional but that it is acquired at sometime between the 17th week of pregnancy and the signs and symptoms of toxæmia."

The consideration of the clinical results and clinical experiments suggest that the sensitizing substance is chorionic gonadotropine rather than oestrogenic hormone or the hormone of the adrenal cortex.

Barnes and Browne, 1945, in concluding a paper on "Blood-pressure and Hypertension", write, "Statistically significant differences could not be found between the mean level of blood-pressure in nulliparous and parous women at any age. Pregnancy does not cause chronic hypertension, the level of blood-pressure in parous women is the same as it would be if they had never been pregnant. Although hypertension is a common sequel of toxæmia of pregnancy, it is not caused by the toxæmia. Patients who develop hypertension following a toxæmic pregnancy would have done so if they had never been pregnant. A tendency to hypertension often contributes to the severity of the toxæmia. There is no evidence that pregnancy permanently aggravates hypertension already existing when pregnancy starts.

Accidental Haemorrhage.

The frequency of accidental haemorrhage in association with eclampsia has been recorded by Bar and Kervily, Convelaire, Essen Möller, Zurate, Scotz, and Young, amongst many others. Gordon Ley, in 1921 in his paper on "Accidental Haemorrhage", writes "Winter in 1885 first directed attention to albuminuria in these cases; since then albuminuria and nephritis has been regarded as the most constantly occurring factor."

It is recorded as occurring:-

in 64.7% of 17 cases by Whitridge Williams.
 in 37.0% of 29 cases by Essen Möller.
 in 50.0% of all his cases by Muns.
 in 42.86% of 70 cases by Gaston.
 in 36.9% of 58 cases by Bar and Kervily.
 in 51.9% of 158 cases by Dorman.
 in 50.75% of 67 cases by Hartmann.

Gordon Ley continues, "One condition only was preeminently associated with accidental haemorrhage, i.e. albuminuria. This association of albuminuria cannot be looked on as an accidental occurrence, and in the absence of other causative factors one naturally looks to the cause of the albuminuria as the cause of the haemorrhage."

Fletcher Shaw says, "The older teaching was that accidental haemorrhage was caused by an accident, but it is very exceptional to see a case even remotely connected with an accident, and a large proportion commence to bleed during the night while in bed. We must look much deeper to find the cause of this condition." He goes on to state, "In my opinion it will be found in some general condition of the patient/

"patient, probably a toxæmia. My chief reason for this belief is founded on the large number of patients with accidental hæmorrhage who have albuminuria which entirely disappears a few days after confinement, not persisting as it does in cases of chronic nephritis."

Gordon Ley says, "The changes in the placenta consist purely of the various stages of infarction."

Essen Möller states that, "The degenerative changes found in the placenta are not characteristic of utero-placental apoplexy but may occur in other conditions as well."

Young states that, "Where a retroplacental hæmorrhage is not quite recent one invariably finds the adjoining placenta diseased, the extent of the necrotic process depending on the length of time the circulation has been cut off. Over old clots we find yellow or white infarcts, and over recent clots, infarction only in its early stages." Young also says, "If part of the placenta remains attached for some hours or days, the circulation there will remain undisturbed, and there will be an opportunity for discharging into the maternal blood stream toxic ingredients quickly elaborated by disintegration of the separated portion; only in such cases will albuminuria or eclampsia develop."

Present Survey.Procedure.

The materials and methods employed in this study were as follows.

One thousand placentae from consecutive deliveries in the normal labour wards, were examined macroscopically, and some sections microscopically.

Each placenta suitably labelled for identification, was gently washed in cold water and after draining it was placed in a prepared 10% solution of Formalin and left there for 48 hours. After fixing in this solution each placenta was thoroughly examined.

The insertion of the umbilical cord was noted (for the purpose of this study the cord insertion was described as Velamentous, Battledore, Paramarginal i.e. anywhere on the outer third of the placenta; Paracentral i.e. anywhere on the middle third of the placenta; Central i.e. anywhere on the central third of the placenta. There were 32.7% Paramarginal, 44.0% Paracentral, 13.0% Central, 10.6% Battledore, 1.2% Velamentous. The fifteen extra were due to twin insertions.

Next any abnormality on the maternal or foetal surface was noted, for example, Succenturiate lobes, of which there were 1.9%; Placenta circumvallata, of which there were 1.0%; Placenta membranacea, of which there were 0.1%; chorionic cysts, five placentae in this series showed chorionic cysts, one placenta had three such cysts. There were 0.4% immature placentae. Retroplacental blood clot was noted and weighed/

weighed.

Each placenta was then stripped of its membranes and umbilical cord; after this the diameter was measured and the whole placenta weighed. Next the placenta was cut in slices of about 1 c.m. in thickness.

Subchorioidal fibrin deposition was noted. Every infarct visible to the naked eye was carefully dissected out and weighed and charted. From representative placenta sections were taken, slides made and examined microscopically.

Placental infarcts, chorionic cysts, etc., were photographed. Some microphotographs were made from a few slides from representative specimens.

Every placenta was drawn on a graph showing diagrammatically the size of the placenta and the size and position of the infarcts.

The clinical histories of these thousand cases were then carefully studied and relevant notes made on a prescribed form. (See Page 26)

The clinical histories and the pathological findings were then correlated, tables were compiled and graphs drawn, and it is the results of these studies which I now wish to present.

It may be of interest to tabulate the chief clinical abnormalities found in the patients in this survey.

Placenta/

Placenta Previa	1.1%	
Eclampsia	0.9%	- 7 antepartum and 2 postpartum
Pre-eclamptic Toxaemia	13.6%	
Ante-partum Haemorrhage	7.4%	
Hypertension	32.8%	
Accidental Haemorrhage	1.5%	- 1.1% Revealed, 0.4% Concealed
Nephritis (chronic)	0.2%	
Pyelitis	2.1%	
Diabetes Mellitus	0.4%	
Tuberculosis	0.6%	

There were 2.2% threatened abortions and 0.3% complete abortions in this series, and 4.3% Stillbirths. Analysis of the causes of the stillbirths is interesting.

Asphyxia 1.3%; Macerated foetus 1.6% (Two Erythroblastosis); Cerebral Haemorrhage 0.7%; Foetal deformities 0.7% i.e.e four were Anencephalic and three had multiple foetal deformities.

There were nineteen mothers in this series with varying degrees of cardiac disease. Three had Hyperemesis Gravidarum, and fifteen others had the following incidental diseases. Thyrotoxicosis 0.5%; Asthma, 0.1%; Haematuria 0.2%; Renal Glycosuria 0.1%; Carcinoma of the Cervix 0.1%; Gonorrhoea 0.1%; Syphilis 0.1%; Epilepsy 0.1%.

Out of the 367 cases in which the Rh. factor was recorded 9.6% were Rh. negative and 27.1% Rh. positive.

The urine analysis for albuminuria in the thousand cases was as follows:-

Negative	79.6%
Trace	10.3%
+	4.8%
++	3.9%
+++	1.4%

Clinical Points.

Patient's Name. Mackintosh, Mrs. Jane.
 Age. 27. Para 0. Ward No. 53.
 P.E.T. Hypertension. Eclampsia. 1 fit.

During Pregnancy.

Infection. P.E.T. (for two weeks before delivery) (One fit just before operation)

Bleeding. --

Blood Pressure. 178/98 (on admission).

Rh. Factor Wife ?
 Husband ?

Albuminuria 3/52:
 (Oedema - Face, hands, legs and feet)

Wassermann Reaction ?

During Delivery. 23.8.47. L.S.C.S.
 D.

Normality of

- 1) Child. Satisfactory (premature 4lbs $\frac{1}{2}$ oz.)
- 2) Placenta. Complete.
- 3) Gestation of Foetus in weeks. 36 + ?

Placenta

Weight 297.6 gms. Diameter 89.10 sq. c.m.
 Area 224.096 sq. c.m.

Infarcts

Number 9. Weight 77.35 gms. Area 58.245 sq.c.m.

Type.

- 1) Fibrin Deposits: Under Chorion:
 Round Circumference.
- 2) True Infarcts: Four "White Infarcts"
 (1 superficial)
 Five "Red Infarcts"
- 3) Haematoma: One.

Observations.

Naked eye examination.
 Insertion of Cord - Para Marginal.
 Placenta - very small. Whole of maternal
 surface showed infarcts. About $\frac{1}{4}$ of
 whole placenta infarcted.

Microscopic Examination

25.821% tissue infarcted.

there was some fibrin deposition under the chorion in 85.6% of the placentae.

Round the Circumference.

There was no fibrin deposit round the circumference in 1.4% of the placentae.

There was a small amount in 91.5%, and a considerable amount in 7.1% of the placentae - i.e. there was some fibrin deposition round the circumference in 98.6% of the placentae.

There was thus some degree of fibrin deposition in 98.6% of all the placentae examined.

True Infarcts.

Due to interference with the maternal circulation, or to some substance circulating in the maternal blood which causes injury to and degeneration of the syncytial layer, with deposition of fibrin encasing the villi, or deposition of fibrin in the intervillous space compressing the villi.

Or the sudden clotting of blood behind, or within the placenta compressing the villi (microscopic examination shows the close packing of the villi, also the fibrin deposition.) The cutting off of the blood supply causes death of the tissue, and thus true infarction.

Red Infarcts.

Red infarcts are recent infarcts, and the first thing visible to the naked eye is just a dark red, purple or nearly black area, distinct from the healthy placental tissue.

When/

When it is a little less recent, this area is somewhat firmer and the outer edge of it has begun to change colour and it sometimes appears to be almost encapsulated. Later still the colour has changed to dark brown or brick-red, and the area is now almost solid. Later on we get what we call white infarcts.

White Infarcts.

The colour is anything from light brown, pink, yellowish, light-grey or almost white.

When cut the area may appear solid, laminated, or granular. This is followed by a slow necrobiosis.

Microscopic examination proves that the change of colour is due to the chemical alterations in the haemoglobin in the blood contained within the affected area.

In my series of 1000 consecutive placentae, there were 427 red infarcts and 2761 white infarcts. Nine of these white infarcts showed degeneration to such an extent that they appeared to be only cavities filled with semifluid gelatinous material.

A typical section showed a central cavity which contained eosinophil staining colloid material surrounded by a wall of hyaline decidual tissue, again surrounded by necrotic chorionic villi.

Other areas showed thrombosis in the intervillous spaces.

True Infarcts.

There were 260 placentae in this series with no infarction visible to the naked eye.

There/

There were 438 placentae each having a small amount of infarction by weight of the infarcts. There were 302 placentae each having a considerable amount of infarction by weight of the infarcts.

27.6% of all the placentae had less than 0.1% of the tissue infarcted.

72.4% of the placentae had more than 0.1% of the placental tissue infarcted.

To summarise the true infarctions in this survey.

26.0% of the placentae - no infarction visible to to the naked eye.

43.8% Each had small amount of infarction.

30.2% Each had a considerable amount of infarction.

In the 438 placentae each having a small amount of infarction there were 1557 separate infarcts.

In the 302 placentae each having a considerable amount of infarction there were 1631 separate infarcts.

The total numbers of infarcts can be shown thus.

3188 infarcts in 740 placentae.

No infarcts in 260 placentae.

∴ 3188 infarcts in 1000 placentae.

The colour of the infarcts in this survey.

White infarcts including different colour changes to white and including nine infarcts with gelatinous degeneration.

White infarcts 2761.

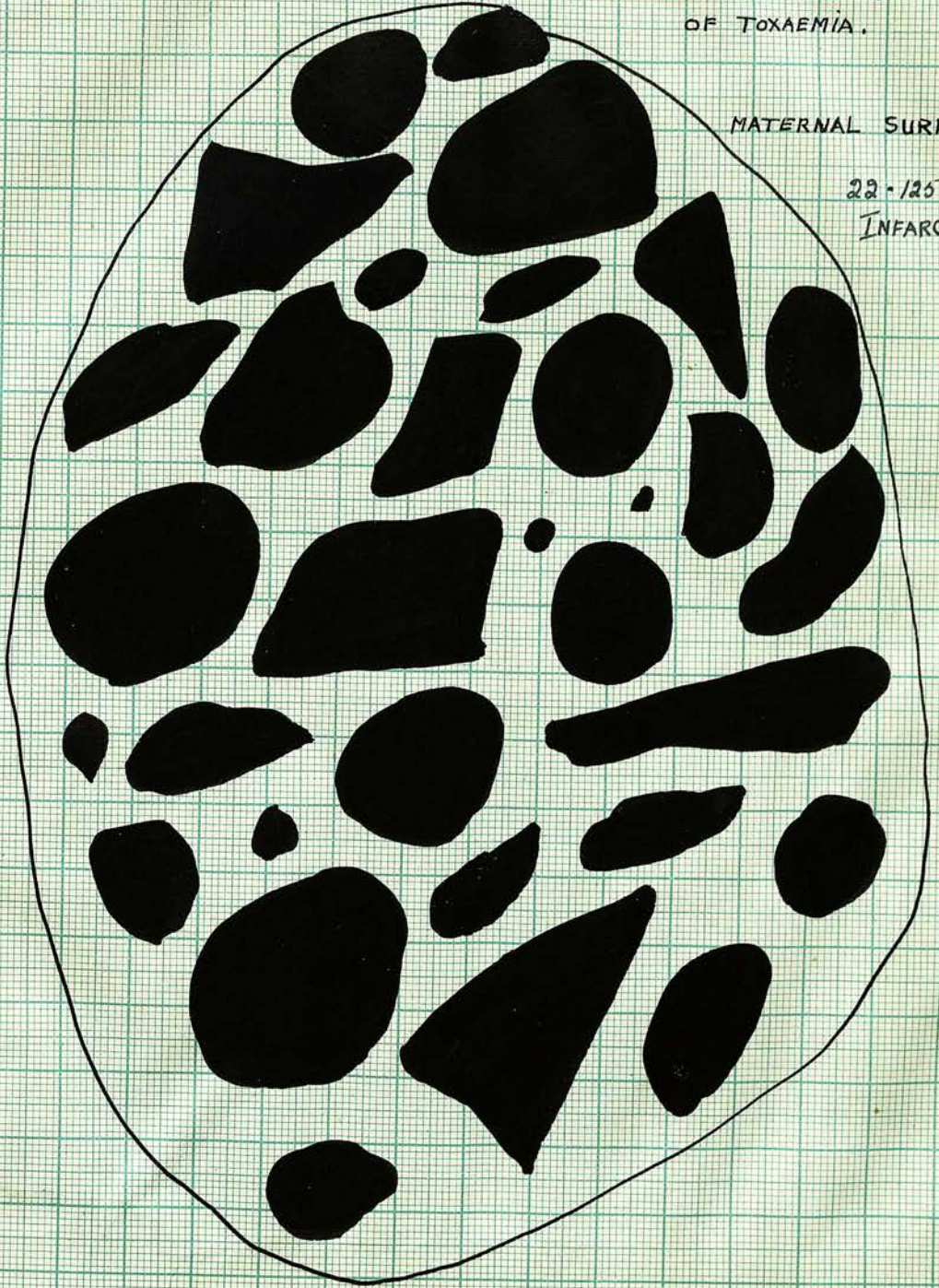
Red infarcts 427.

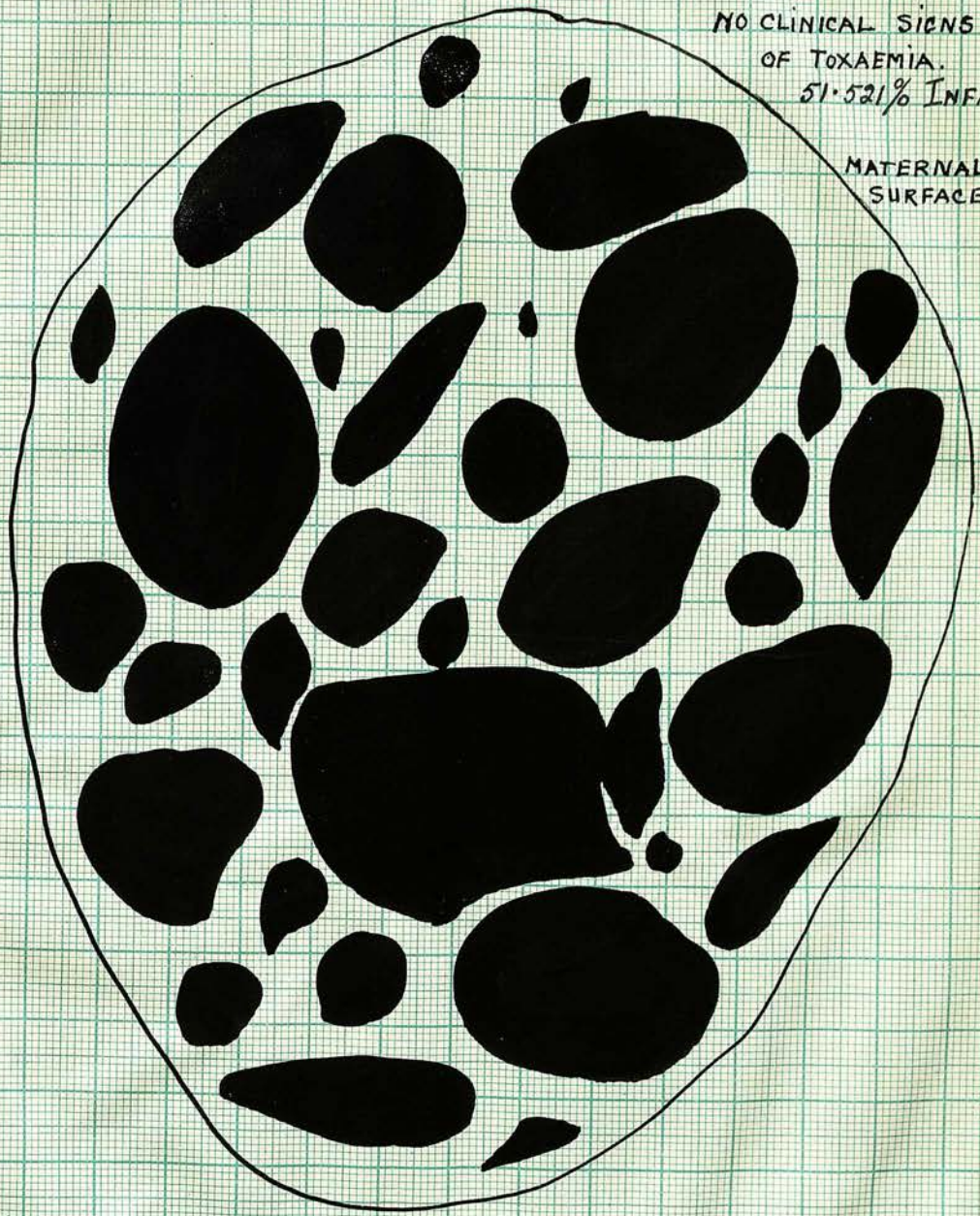
∴ 3188 infarcts in 1000 placentae.

NO CLINICAL SIGNS
OF TOXAEMIA.

MATERNAL SURFACE.

22.125%
INFARCTION.





NO CLINICAL SIGNS
OF TOXAEMIA.
51.521% INFARCTION.

MATERNAL
SURFACE.

Haematomata.

- A. Retroplacental blood clot.
- B. Intraplacental blood clot.

A. Retroplacental blood clot is almost always due to accidental haemorrhage, often causing definite depressions on the maternal surface of the placenta, the immediately underlying villi are compressed and usually necrotic depending on the length of time the pressure has lasted.

B. Intraplacental blood clot is possibly due to obstruction in the decidual veins, pressure of the blood causing rupture in the thin distended vein, and escape of blood into the soft tissue. These clots are also usually surrounded by a layer of necrotic placental tissue.

In this series there were eleven retroplacental blood clots and two hundred and thirty nine intraplacental blood clots.

Some of the haematomata were very small, others were larger, some quite large.

The haematomata may be summarised thus.

In 750 of the placentae there were no haematomata.

In 239 of the placentae there were "Intraplacental haematomata".

In 11 of the placentae there were "Retroplacental haematomata".

Intraplacental haematomata 23.9%

Retroplacental haematomata 1.1%

Total haematomata 250 in 1000 placentae.

Pre-eclamptic Toxaemia and Eclampsia.Pre-eclamptic Toxaemia.

In this survey 136 of the 1000 mothers had clinical signs of pre-eclamptic toxaemia.

Many of these had been treated in hospital antenatally and the condition very much improved.

It was noticed that where there was only a mild degree of pre-eclamptic toxaemia the placenta was healthy, or only slightly "infarcted", but where there was a severe degree of toxaemia there was likely to be more infarction in the placenta.

In the following groups of cases of mild pre-eclamptic toxaemia I have set out figures showing the percentage of infarction, the blood pressure range, albuminuria, and the duration range of clinical symptoms.

Group 1.

No infarction of the placenta visible to the naked eye. 21 cases.

Blood pressure range. Highest 160/85. Lowest 120/80.

Duration of clinical symptoms. 1-4 weeks.

Albuminuria.

In 10 cases negative; in six cases a trace; in two cases +; in 1 case ++; in two cases +++ albumin.

Group 11.

Average Infarction 1.5% by weight. 13 cases.

Blood pressure range. Highest 160/75. Lowest 120/80.

Duration/

Duration of clinical symptoms. 1-3 weeks.

Albuminuria.

In 4 cases negative; in five cases a trace; in two cases + ; in one case ++ ; in 1 case +++ albumin.

Group III.

Average Infarction 2.5% by weight. 15 cases.

Blood pressure range. Highest 170/110. Lowest 125/90.

Duration of clinical symptoms. 1-4 weeks.

Albuminuria.

In 7 cases negative; in 3 cases a trace; in 2 cases + ; in 1 case ++ ; in 1 case +++ albumin.

Group IV.

Average Infarction 3.5% by weight. 13 cases.

Blood pressure range. Highest 175/70. Lowest 130/80.

Duration of clinical symptoms. 2-4 weeks.

Albuminuria.

In 7 cases negative; in 3 cases a trace; in 3 cases ++ albumin.

Group V.

Average Infarction 4.5% by weight. 7 cases.

Blood pressure range. Highest 160/90. Lowest 138/90. Duration of clinical symptoms. 2-8 weeks.

Albuminuria.

In 3 cases negative; in 3 cases a trace; in 1 case ++ albumin.

Group VI.

Average/

Group VI.

Average Infarction 5.5% by weight. 10 cases.

Blood pressure range. Highest 170/120. Lowest 110/80.

Duration of clinical symptoms. 3-8 weeks.

Albuminuria.

In 4 cases negative; in 1 case a trace; in 1 case + ; in 4 cases ++ albumin.

Group VII.

Average Infarction 6.5% by weight. 7 cases.

Blood pressure range. Highest 156/100. Lowest 140/90.

Duration of clinical symptoms. 3-4 weeks.

Albuminuria.

In 1 case negative; in 4 cases a trace; in 2 cases + albumin.

Group VIII.

Average Infarction 8.5% by weight. 6 cases.

Blood pressure range. Highest 180/110. Lowest 120/70.

Duration of clinical symptoms. 3-8 weeks.

Albuminuria.

In 1 case negative; in 1 case a trace; in 3 cases + ; in 1 case ++ albumin.

Group IX.

Average Infarction 9.5% by weight. 4 cases.

Blood pressure range. Highest 140/100. Lowest 120/75.

Duration/

Duration of clinical symptoms. 2-6 weeks.

Albuminuria.

In 1 case negative; in 2 cases a trace; in 1 case + albumin.

In the groups of cases of severe pre-eclamptic toxæmia the figures are set out in the same manner.

Group I.

Average Infarction 7.5% by weight. 2 cases.

Blood pressure range. Highest 180/120. Lowest 165/100.

Duration of clinical symptoms. 1 week.

Albuminuria.

In 1 case + ; in 1 case ++ albumin.

Group II.

Average Infarction 8.5% by weight. 3 cases.

Blood pressure range. Highest 200/138. Lowest 180/110.

Duration of clinical symptoms. 2-8 weeks.

Albuminuria.

In 3 cases +++ albumin.

Group III.

Average Infarction 10.5% by weight. 3 cases.

Blood pressure range. Highest 160/100. Lowest 135/95.

Duration of clinical symptoms. 2-8 weeks.

Albuminuria.

In 2 cases a trace. In 1 case + albumin.

Group IV/

Group IV.

Average Infarction 11.5% by weight. 1 case.

Blood pressure 180/100.

Duration of clinical symptoms. 8 weeks.

Albuminuria. ++ albumin.

Group V.

Average Infarction 12.5% by weight. 3 cases.

Blood pressure range. Highest 170/100. Lowest 160/98.

Duration of clinical symptoms. 3-4 weeks.

Albuminuria.

In 1 case a trace; in 1 case + ; in 1 case ++ albumin.

The following 15 cases I will report separately to bring out some special points.

1. This case had mild pre-eclamptic toxæmia from the 7th to 16th week of pregnancy treated in hospital. She was again admitted in the 32nd and 36th weeks of pregnancy for a few days each time.

The average blood pressure was 150/90.

Albuminuria. + albumin.

There was 10.982% of the placental tissue infarcted. A case of long-standing very mild pre-eclamptic toxæmia. The mother was delivered of a stillborn macerated foetus.

11. This case had mild pre-eclamptic toxæmia throughout pregnancy, also pyelitis from the 4th - 17th day/

day of her 8th month of pregnancy.

The average blood pressure was 160/100.

Albuminuria. + albumin.

There was 13.523% of the placental tissue infarcted.

A case of long-standing mild pre-eclamptic toxæmia.

III. This case gave a history of clinical symptoms of pre-eclamptic toxæmia for just one week before delivery.

Blood pressure average 160/100.

Albuminuria. ++ albumin.

There was 18.95% of the placental tissue infarcted.

The mother was delivered of a premature infant at 37th week.

IV. This case had symptoms of clinically mild pre-eclamptic toxæmia for one month before delivery.

Blood pressure average 154/100.

Albuminuria. ++ albumin.

There was 19.08% of the placental tissue infarcted.

V. This case had clinical symptoms of severe pre-eclamptic toxæmia for 5 weeks + before delivery.

Blood pressure average 165/100.

Albuminuria. +++ albumin.

There was 21.721% of the placental tissue infarcted.

Severe toxæmia for over five weeks.

VI. This case showed no clinical signs of pre-eclampsia.

Blood pressure on admission - 160/100.

Albuminuria. Negative for albumin.

The mother had a complete placenta previa.

There was 22.12% of the placental tissue infarcted.

Vll. This case showed no clinical signs or symptoms of pre-eclamptic toxæmia.

No history of raised blood pressure.

Albuminuria. Negative for albumin.

There was 22.125% of the placental tissue infarcted.

Vlll. This case showed clinical symptoms of very mild pre-eclamptic toxæmia for 4 months.

The average blood pressure was 138/85.

Albuminuria. Negative for albumin.

There was 22.35% of the placental tissue infarcted.

A case of very long, very mild toxæmia.

lX. This case showed clinical signs and symptoms of pre-eclamptic toxæmia for only two days before delivery.

Had a history of blood pressure 145/100 for two weeks.

Albuminuria. ++ albumin for two days.

There was 23.7% of the placental tissue infarcted.

A case of mild pre-eclamptic toxæmia of short clinical duration.

X. This case showed clinical signs and symptoms of severe pre-eclamptic toxæmia for more than a month.

The average blood pressure 200/140.

Albuminuria. ++ albumin.

The mother had profuse antepartum hæmorrhage. She was delivered of a stillborn macerated foetus at 32nd week.

There was 41.2% of the placental tissue infarcted.

XI. This case had no history of any clinical signs or symptoms of toxæmia.

No history of raised blood pressure.

Albuminuria. Negative for albumin.

There was 51.521% of the placental tissue infarcted.

(? Subclinical toxæmia of long-standing.)

XII. This case had clinical symptoms of mild pre-eclamptic toxæmia for over four months.

Blood pressure on admission 170/100.

Albuminuria. No history.

There was 60.925% of the placental tissue infarcted.

A case of mild toxæmia of long duration.

XIII. This case had clinical symptoms of moderately severe pre-eclamptic toxæmia for six weeks before delivery.

Blood pressure average, 175/100.

Albuminuria. +++albumin.

She had only 2.621% of the placental tissue infarcted but she had one postpartum eclamptic fit.

XIV. This case had clinical symptoms of severe pre-eclamptic toxæmia for one month before delivery.

Albuminuria. ++ albumin.

The mother was delivered at the 29th week of pregnancy of a macerated foetus. A case of missed abortion.

There was 95% of placental tissue infarcted. Only a few strands of placental tissue could be distinguished between the infarcts (see photograph and graph).

XV.

XV. This is a case of Chronic Nephritis, with raised blood pressure throughout pregnancy - average 140/90.

Albuminuria. +++ albumin.

The mother was delivered of a stillborn macerated foetus at the 27th week of pregnancy.

There was 48.535% of the placental tissue infarcted. (See photograph and graph.)

A study of the foregoing cases seems to bring out the following facts.

1. A mild toxæmia of about one month's duration will result in very little or no infarction of the placenta.

2. A mild toxæmia of long duration will result in massive infarction of the placenta.

3. A severe toxæmia of about one month's duration will result in massive infarction of the placenta.

4. Severe toxæmia does not have a long duration.

In 21 of the 136 placentae from cases of pre-eclamptic toxæmia there were no infarcts visible to the naked eye.

Another 7 of the 136 placentae had less than 1.0% each, by weight, of "infarcted tissue".

Did the prompt treatment of early signs and symptoms of pre-eclamptic toxæmia prevent many of these placentae from being severely "infarcted"? I believe it did.

Eclampsia.

There were seven antepartum and three postpartum cases of eclampsia in nine mothers of this series of a thousand cases. Of these nine placentae two showed no infarction visible to the naked eye.

I. This case had a history of clinical signs and symptoms of pre-eclamptic toxæmia for one month before delivery.

Blood pressure average 180/100 for three weeks.

There was no infarction of placental tissue visible to the naked eye.

The mother had two eclamptic fits before admission.

II. This case had no history of any signs or symptoms of pre-eclamptic toxæmia. She said she felt well until the day of her delivery.

Blood pressure on admission - 170/110.

There was no infarction of placental tissue visible to the naked eye.

The mother had three eclamptic fits on the day of delivery. She was delivered of a premature infant at the 36th week.

III. This case had no history of any clinical signs or symptoms of pre-eclamptic toxæmia. No history of raised blood pressure.

There was only 1.0% of placental tissue "infarcted".

The mother had one eclamptic fit on day of delivery at full term.

IV. This case had a history of clinical signs and symptoms/

symptoms of mild pre-eclamptic toxæmia for six weeks.

Blood pressure average - 175/100.

She was delivered at full term.

There was 2.621% of the placental tissue "infarcted".

The mother had one eclamptic fit, postpartum.

V. This case had clinical signs and symptoms of severe pre-eclamptic toxæmia for ten days.

Blood pressure average - 180/110.

There was 4.612% of the placental tissue "infarcted".

The mother was delivered of a premature infant at 37 weeks. She had one eclamptic fit antepartum and four eclamptic fits postpartum.

V1. This case gave a history of feeling perfectly well all throughout her pregnancy, although her doctor had put her to bed for the past six weeks.

Blood pressure average - 190/110.

There was 5.9% of the placental tissue "infarcted".

She was delivered at full term and had one eclamptic fit during the puerperium.

V11. This case had a history of clinical signs and symptoms of pre-eclamptic toxæmia for three weeks before admission.

Blood pressure average - 120/90.

There was 8.699% of the placental tissue "infarcted".

The mother was delivered of a premature infant at 31st week. She had four eclamptic fits antepartum.

V111. This patient had a history of clinical signs and symptoms of pre-eclamptic toxæmia for three weeks before/

before admission.

Blood pressure average - 166/100.

There was 14.81% of the placental tissue "infarcted".

The mother was delivered of a premature infant at the 39th week. She had one eclamptic fit antepartum.

1X. This patient had a history of pre-eclamptic toxæmia for two weeks before delivery.

Blood pressure average - 178/98 for three weeks.

There was 25.821% of the placental tissue "infarcted".

The mother was delivered of a premature infant at the 26th week. She had one eclamptic fit antepartum.

All the patients except numbers 4 and 6 had eclamptic fits on the day of delivery, but all made a satisfactory recovery. All the babies were born alive.

A study of the percentage weight of infarction in these nine placentae reveals the fact that two of them had no infarction visible to the naked eye, and only numbers 8 and 9 had a considerable amount of the tissue "infarcted".

Nine placentae are too few to base any dogmatic statement on, but for this small number at least it shows that the eclampsia was not the result of massive infarction of the placentae.

Young states that the extent of the necrotic process is determined by the length of time the circulation has been cut off.

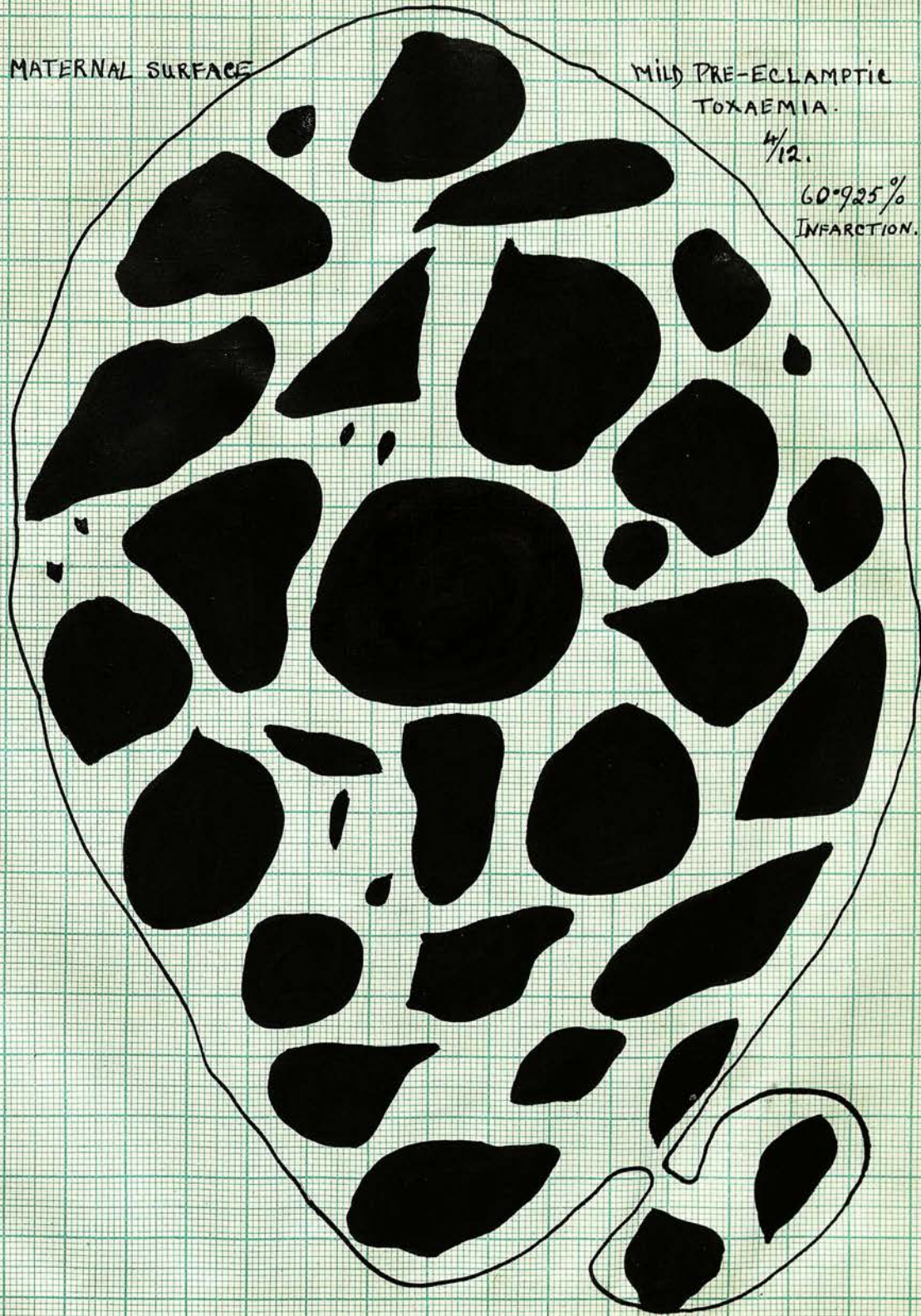
It may be that in eclampsia there are infarcts too small to be visible to the naked eye.

MATERNAL SURFACE

MILD PRE-ECLAMPTIC
TOXAEMIA.

4/12.

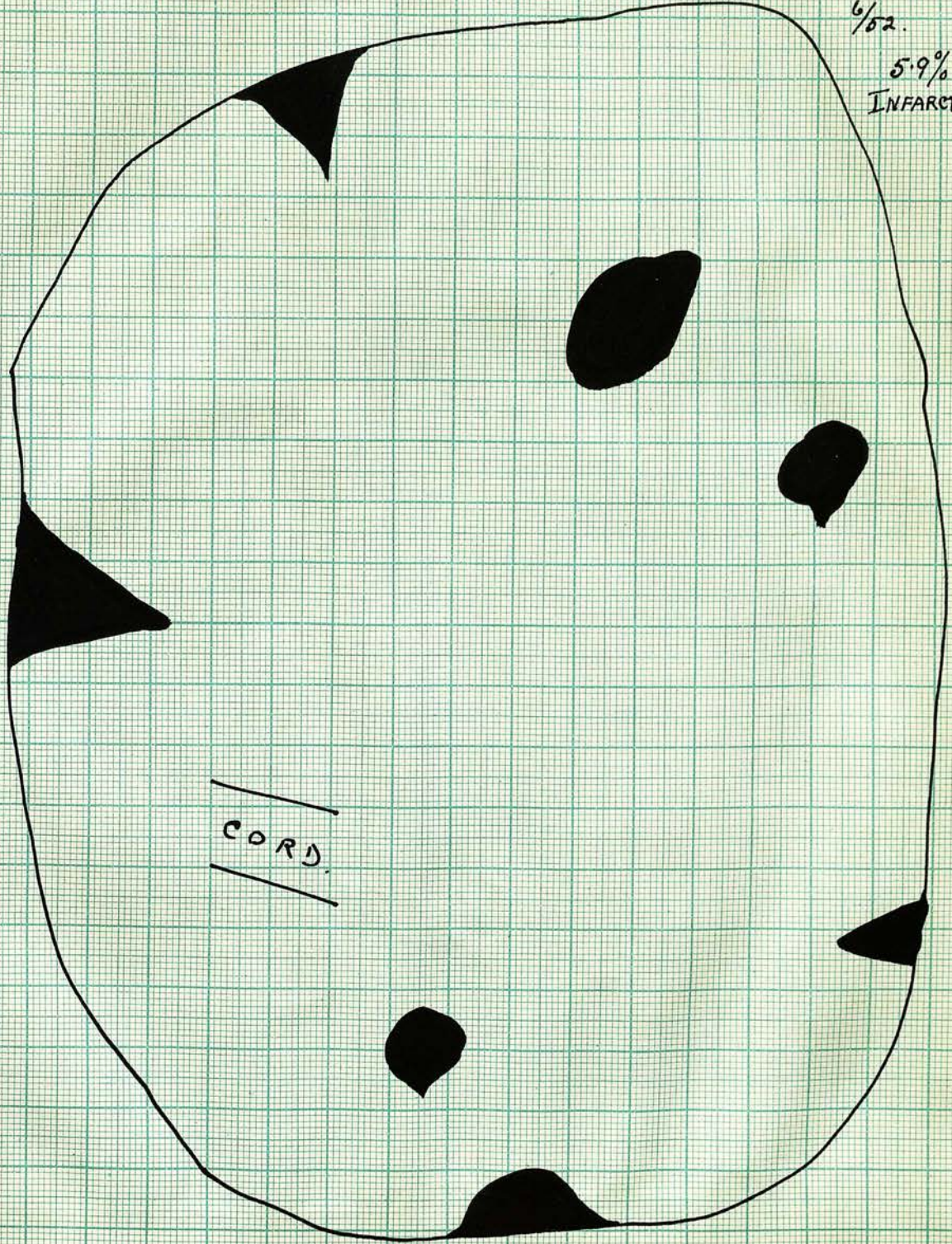
60-925%
INFARCTION.



MODERATELY.
SEVERE PRE-ECLAMPTIC TOXAEMIA.

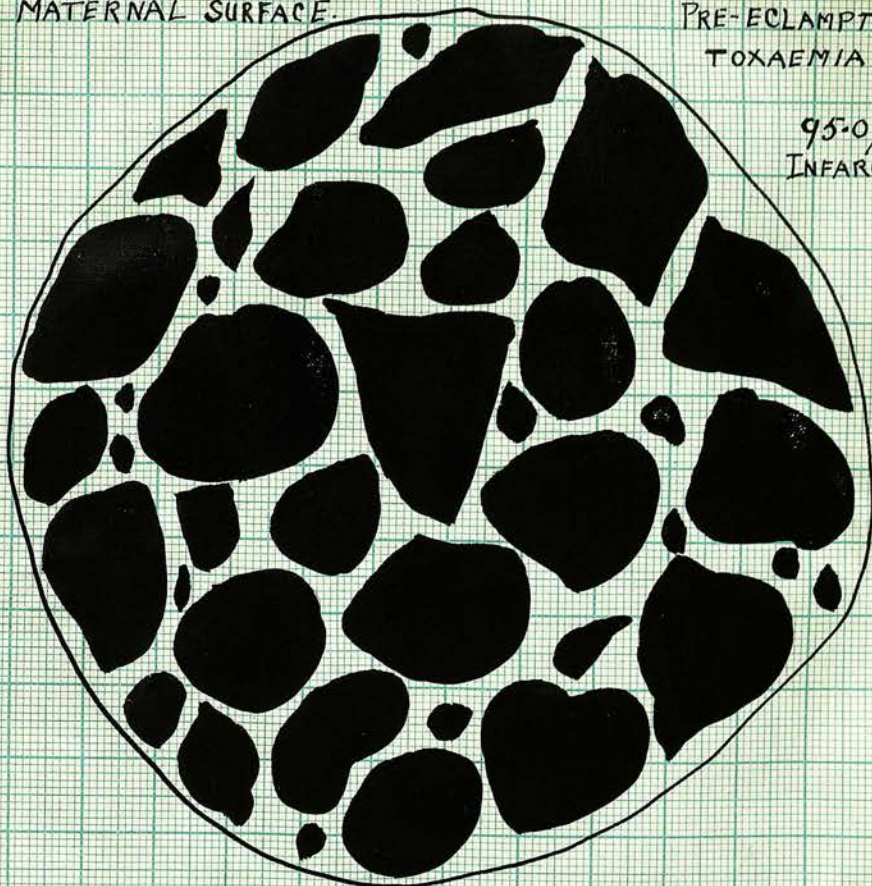
6/82.

5.9%
INFARCTION.



CORD

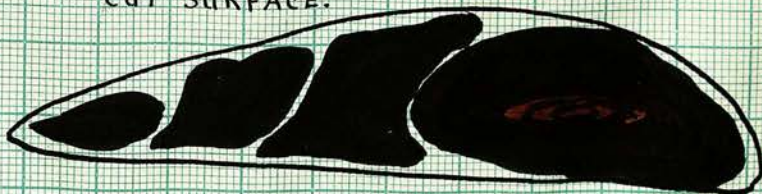
MATERNAL SURFACE.



SEVERE
PRE-ECLAMPTIC
TOXAEMIA. $\frac{1}{12+}$.

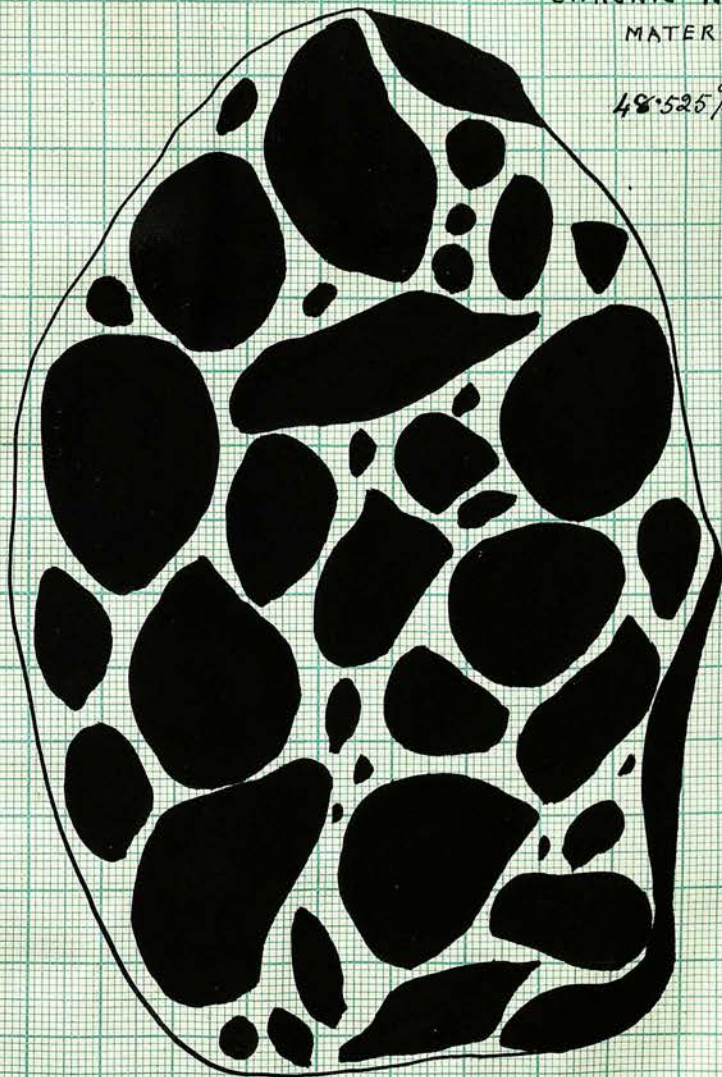
95.0%
INFARCTION.

CUT SURFACE.



CHRONIC NEPHRITIS.
MATERNAL SURFACE.

48.525% INFARCTION.



Cut sections from case of severe Pre-eclamptic
Toxaemia.

Case XIV.



No normal placental tissue to be seen.
Infarcted tissue, in all stages, well seen.
95% of the placental tissue was infarcted.
Duration of pregnancy 29 weeks.
Foetus dead for some time - missed abortion.

Maternal Surface. Case XIV.



Placenta from a case of severe Pre-eclamptic Toxaemia.

Great masses of infarcted tissue seen.



Cut sections of placenta from case of
Chronic Nephritis.
Case XV.



Practically no normal placental tissue seen.
Infarction in all its stages, well seen.
48.525% of the placental tissue was
infarcted.
Duration of pregnancy 27 weeks.
Foetus dead born, macerated. 1st pregnancy.

Maternal Surface. Case XV.



A very small placenta from a case of Chronic Nephritis.

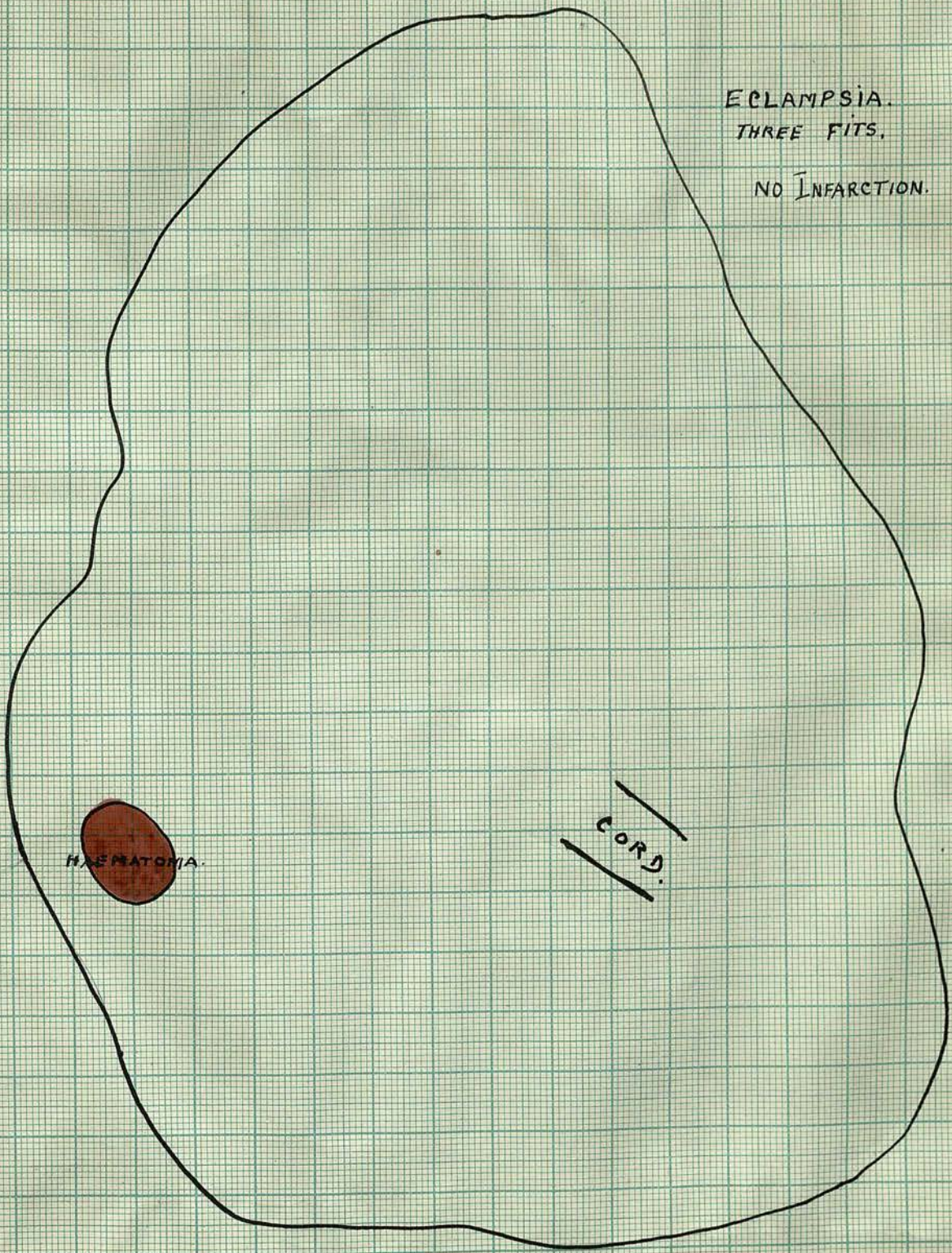
The whole organ practically a mass of infarcted tissue.

ECLAMPSIA. Two Fits.

NO INFARCTION.

CORD.

ECLAMPSIA.
THREE FITS.
NO INFARCTION.

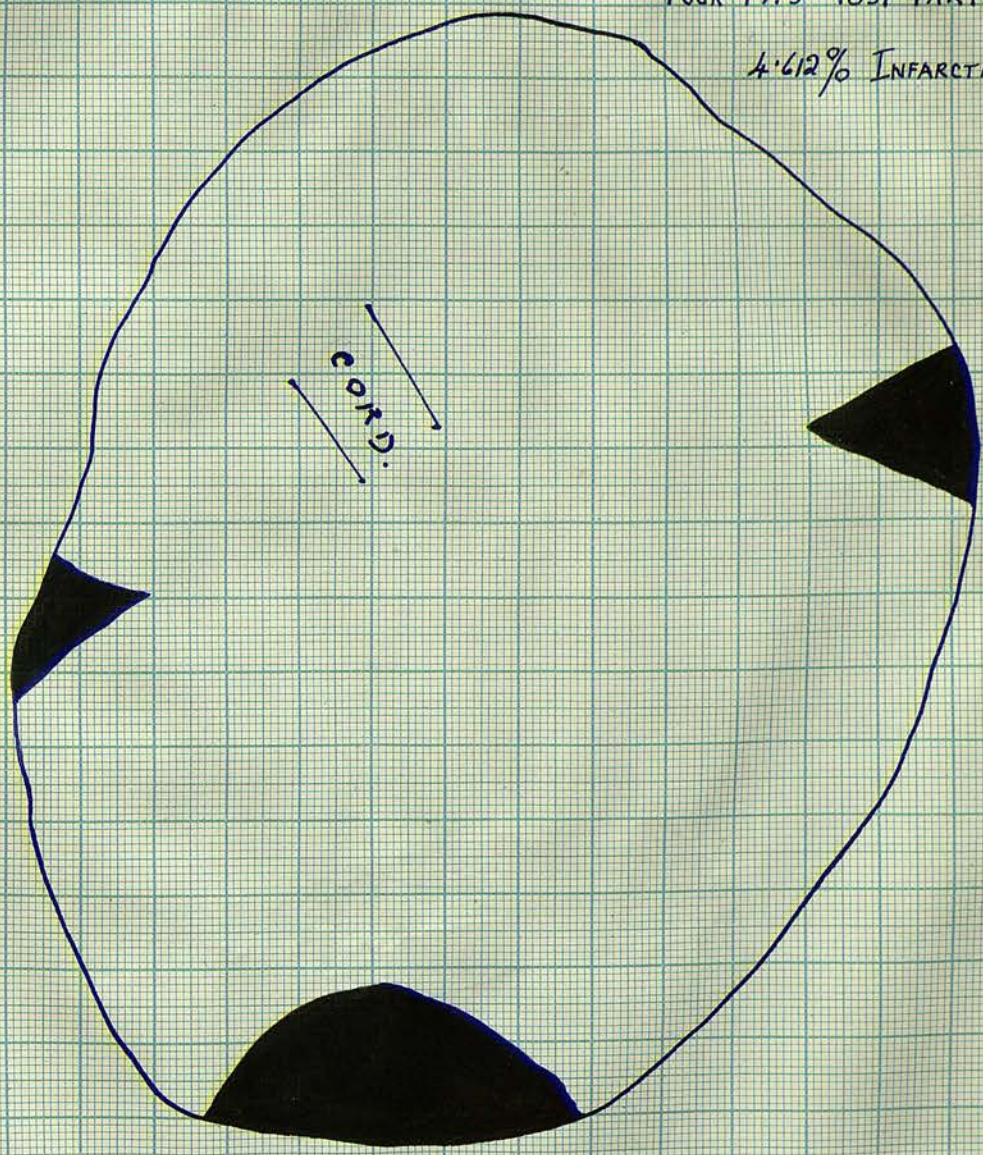


HEMATOMA.

CORD.

ECLAMPSIA.
ONE FIT ANTE-PARTUM.
FOUR FITS POST-PARTUM.

4.62% INFARCTION.



ECLAMPSIA.
FOUR FITS.

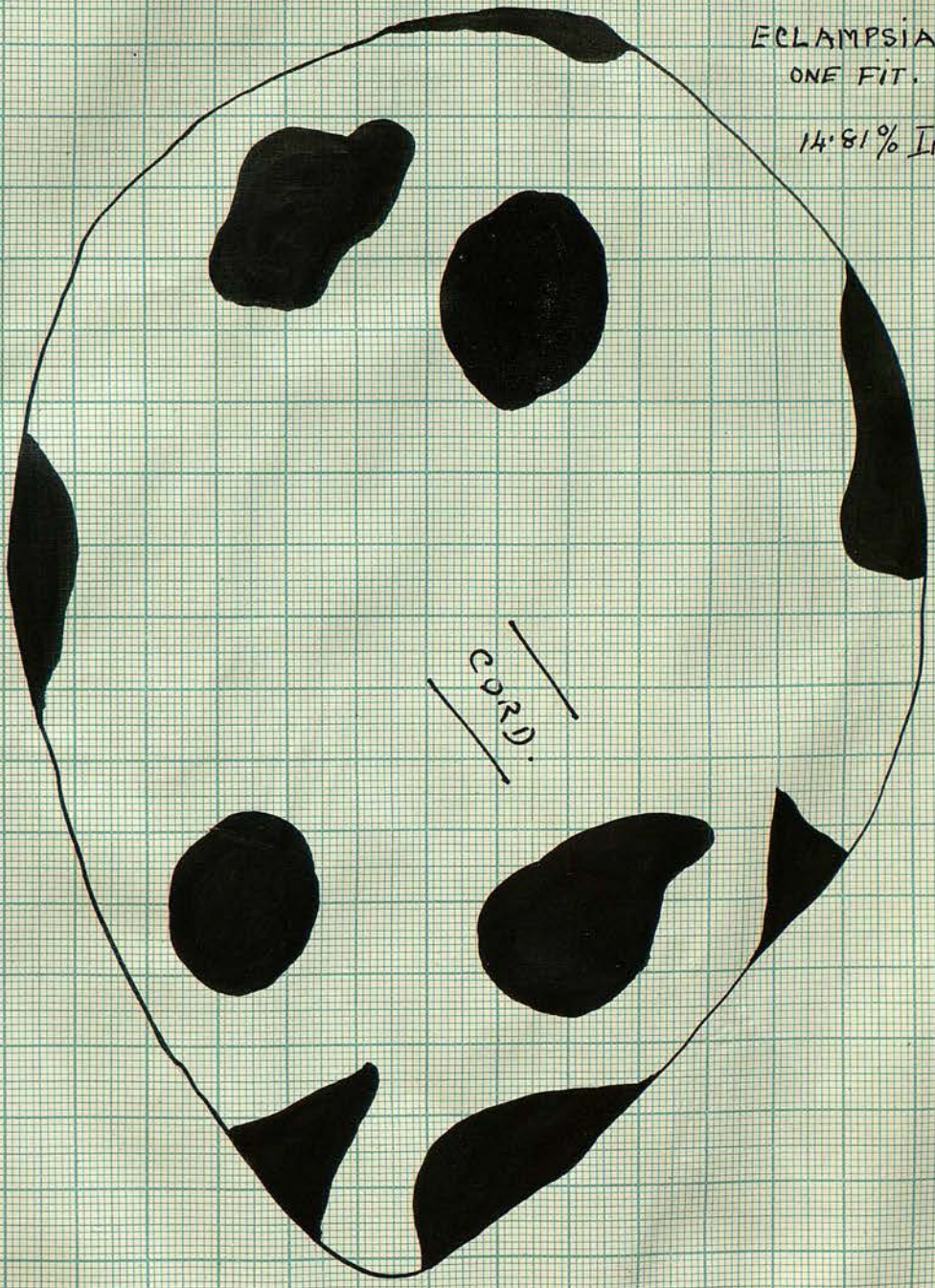
8.699% INFARCTION.



CORD.

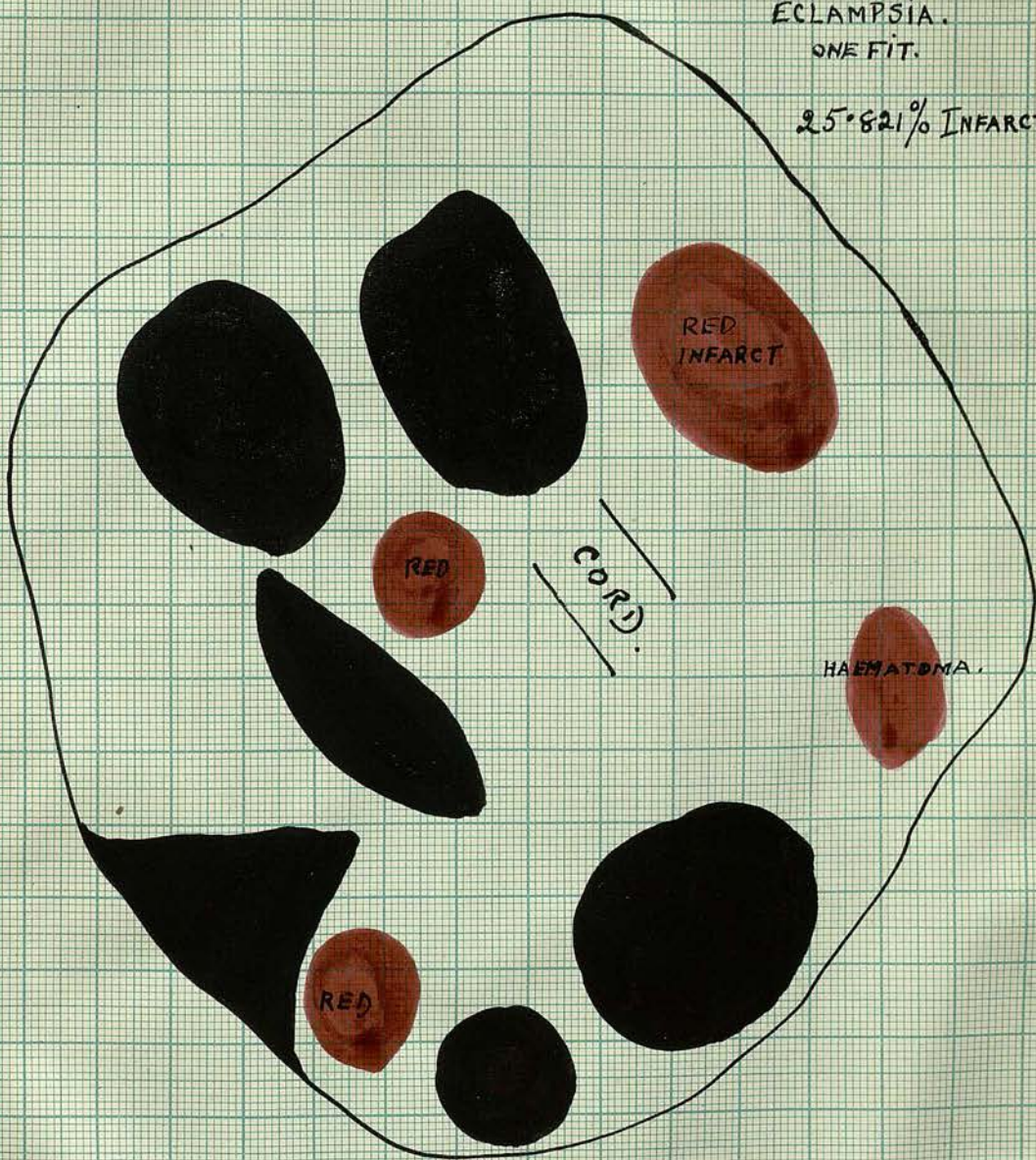
ECLAMPSIA.
ONE FIT.

14.81% INFARCTION.



ECLAMPSIA.
ONE FIT.

25.821% INFARCTION.



Hypertension.

In this survey of one thousand cases of consecutive deliveries in hospital the majority had been attending antenatal clinics, and the blood pressure readings were observed there, but many cases came into the hospital from outside districts already in labour, and for many of these latter no antenatal record of blood pressure readings could be procured.

From the data it is calculated that out of the thousand cases, 328 patients had hypertension calculated from a systolic blood pressure of over 130 m.m. of Hg. on any one occasion during pregnancy. 136 of these patients showed some signs of pre-eclamptic toxæmia, while the other 192 patients showed some degree of hypertension only. Of these 328 cases showing hypertension 72 had no visible naked eye infarcts in the placenta. A further 14 had less than 1.0% by weight of "infarcted tissue" in the placenta. (For percentage distribution see graph H. also Table 2.)

During this study I noticed that where hypertension had only lasted for a short time the placenta was likely to be healthy but where the hypertension had lasted for a long time the placenta was more likely to be infarcted. The length of time rather than the height of the mercury seemed to matter most in the production of infarction of the placenta. The following details corroborate this impression.

In this survey there were five cases of essential hypertension.

1. This patient had a blood pressure average of 158/100 throughout/

throughout pregnancy with slight oedema of the hands and ankles. There was 9.5% of the placental tissue "infarcted".

11. This patient had a blood pressure average of 140/90 throughout pregnancy; she did not have any signs or symptoms of toxæmia. There was 5.3% of tissue "infarcted".

111. This patient had a blood pressure average of 150/110 throughout pregnancy, she had slight oedema of the ankles; there was 4.2% of the placental tissue "infarcted".

1V. This patient had a blood pressure average of 160/112 throughout pregnancy. She did not have any signs or symptoms of toxæmia. There was 3.3% of the placental tissue "infarcted".

V. This patient had a blood pressure average of 150/90 throughout pregnancy. She did not have any signs or symptoms of toxæmia. There was no infarction of the placenta visible to the naked eye.

In this small number there does not appear to have been any maternal disturbance during the pregnancy nor any great infarction of the placenta, caused by the essential hypertension.

Hypertension.

72 patients in this series had varying degrees of hypertension with no infarction of the placenta visible to the naked eye. The majority of them had hypertension of less than one month's duration.

One patient had a blood pressure average of 160/100 for five/

five months, she did not have any signs or symptoms of toxæmia and there was no infarction of the placenta visible to the naked eye.

There were 12 patients with a blood pressure average each of 140/90 - 150/100 on admission to hospital, with no previous history of hypertension, who had from 2.0% - 16.0% of the placental tissue "infarcted".

Whereas a case of Chronic Nephritis with a blood pressure range of 140/90 throughout pregnancy had 48.525% of the placental tissue "infarcted".

A group of 8 patients with histories of hypertension for three weeks, with blood pressure average 140/85 - 175/100 had from 3.0% - 7.0% of the placental tissue "infarcted".

A group of 40 patients with histories of hypertension for over one month and under two months duration, with blood pressure average 130/85 - 190/110, had from 2.5% - 22.0% of the placental tissue "infarcted".

A group of 6 patients with histories of hypertension of from four months to six months duration, with blood pressure average 138/85 - 170/100 had from 13.5% - 60.9% of the placental tissue "infarcted".

Although the numbers of cases in each group are small the study shows a definite increase in the percentage of placental tissue "infarcted" the longer the duration of the hypertension.

38.

Accidental Haemorrhage.

In this survey, out of a thousand consecutive deliveries there were 15 cases of Accidental Haemorrhage. 11 were cases of revealed accidental haemorrhage and 4 were cases of concealed accidental haemorrhage.

Of the four cases of concealed accidental haemorrhage one had neither hypertension nor albuminuria. Three had both hypertension and albuminuria. None of the four mothers had pre-eclamptic toxæmia but all four babies were born dead. All the mothers made a satisfactory recovery.

Of the eleven cases of revealed accidental haemorrhage, all the mothers had hypertension, three had pre-eclamptic toxæmia with hypertension and albuminuria, one had hypertension and albuminuria, and seven had hypertension only. Ten of the babies were born alive, one baby was born dead. All the mothers made a satisfactory recovery.

There were two cases of accidental haemorrhage with no placental infarction visible to the naked eye.

There were four cases with less than 2.5% of the placental tissue "infarcted".

There were two cases with less than 6.5% of the placental tissue "infarcted".

There were two cases with 10.5% of the placental tissue "infarcted".

One case had 12.175% of the placental tissue "infarcted".

One case had 15.35% of the placental tissue "infarcted".

The above cases all had slight hypertension, but none of them showed any other signs or symptoms of toxæmia/

toxaemia.

There were three cases of accidental haemorrhage who also had signs and symptoms of severe pre-eclamptic toxaemia.

1. This case had clinical signs and symptoms of severe pre-eclamptic toxaemia of three weeks duration. Blood pressure 130/85. Albumin in urine + . Oedema of labia +++ . Profuse haemorrhage. There was 18.9% of the placental tissue "infarcted".

2. This case had clinical signs and symptoms of severe pre-eclamptic toxaemia for more than one month. Blood pressure 200/140. Albumin in urine ++ . Profuse haemorrhage.

There was 41.2% of the placental tissue "infarcted".

3. This case had signs and symptoms of severe pre-eclamptic toxaemia on admission. No history of its duration. Blood pressure 190/100 on admission. Small concealed haemorrhage.

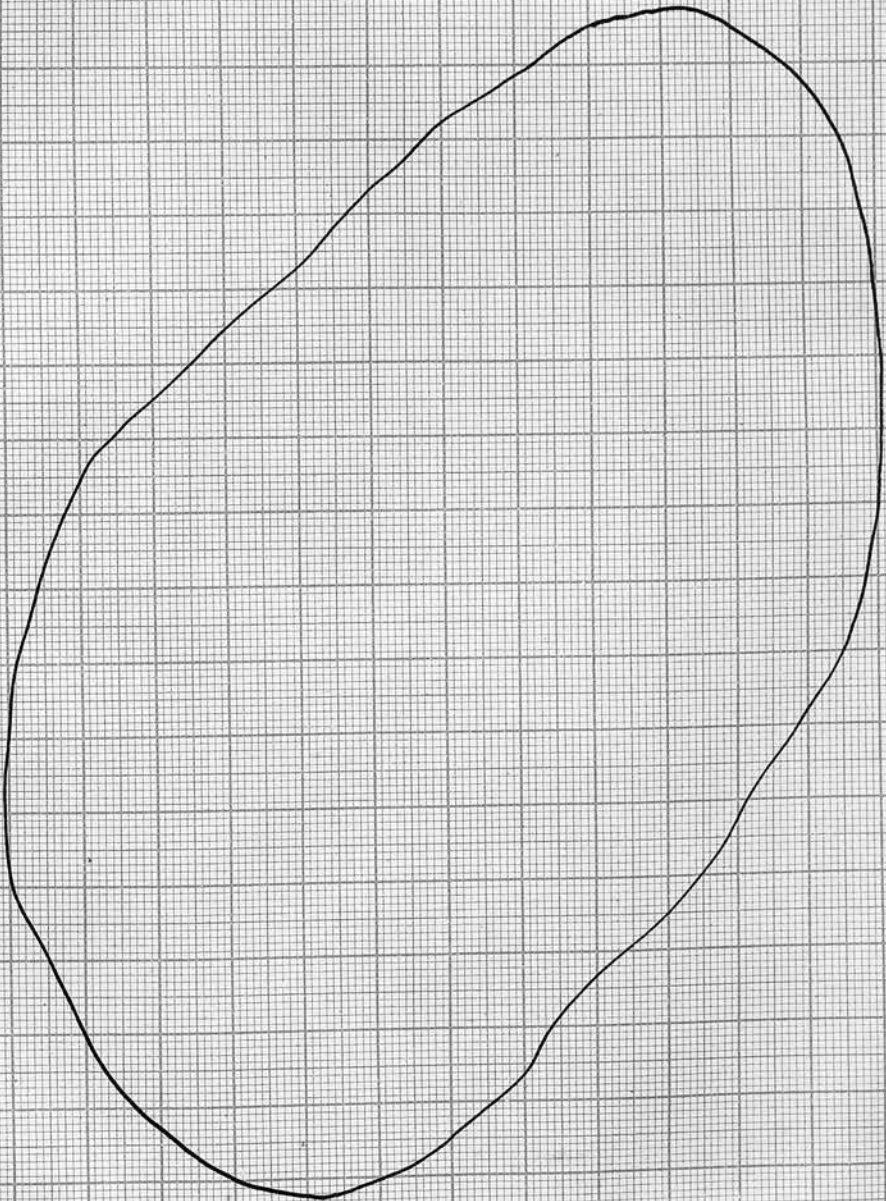
There was 60.98% of the placental tissue "infarcted".

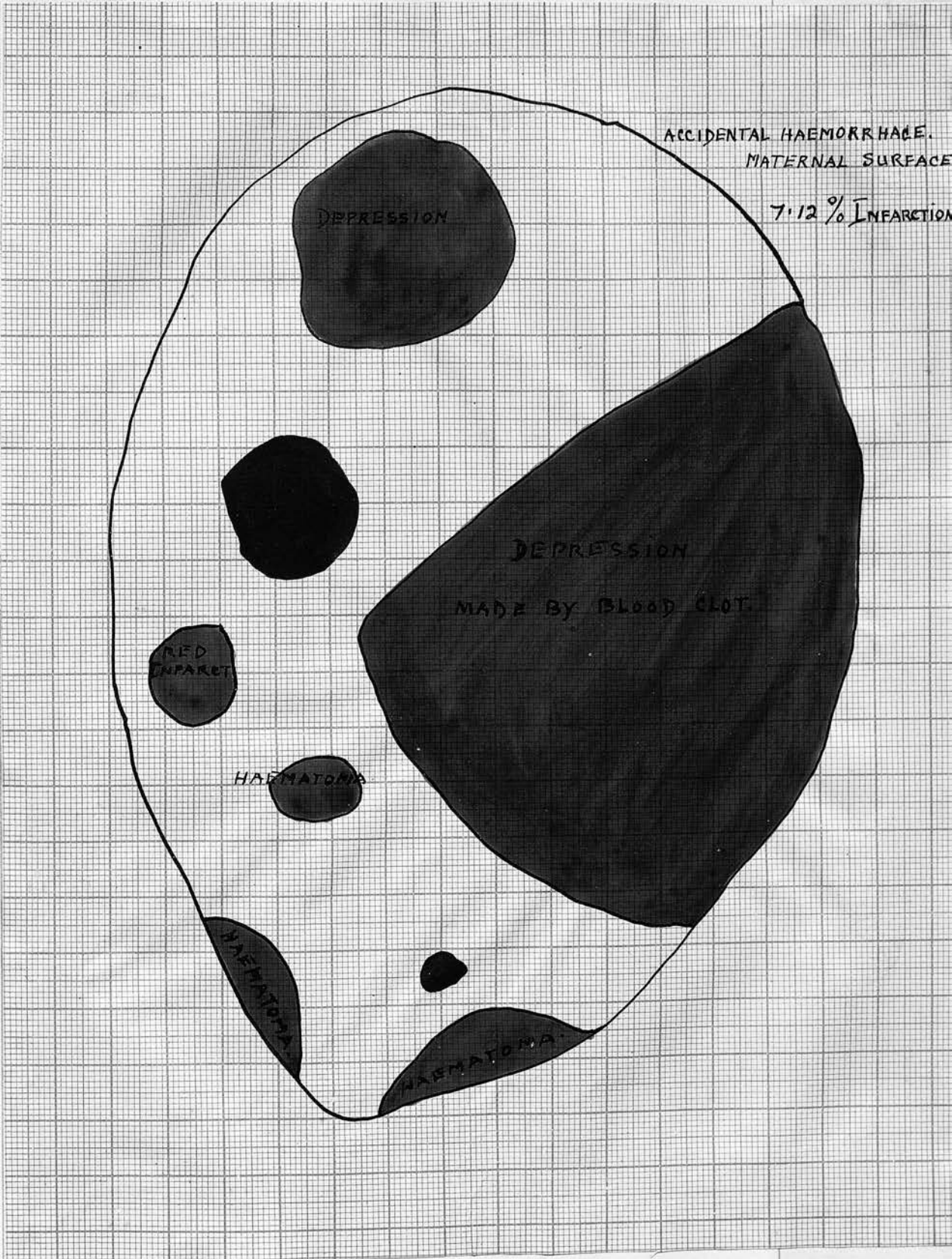
The study of this small group of cases of accidental haemorrhage reveals the following facts.

1. Of twelve cases, uncomplicated by pre-eclamptic toxaemia, only two showed any considerable amount of infarction of the placenta while two cases showed no infarction of the placenta visible to the naked eye.

11. The three cases of accidental haemorrhage complicated by severe pre-eclamptic toxaemia, all had massive infarction of the placenta.

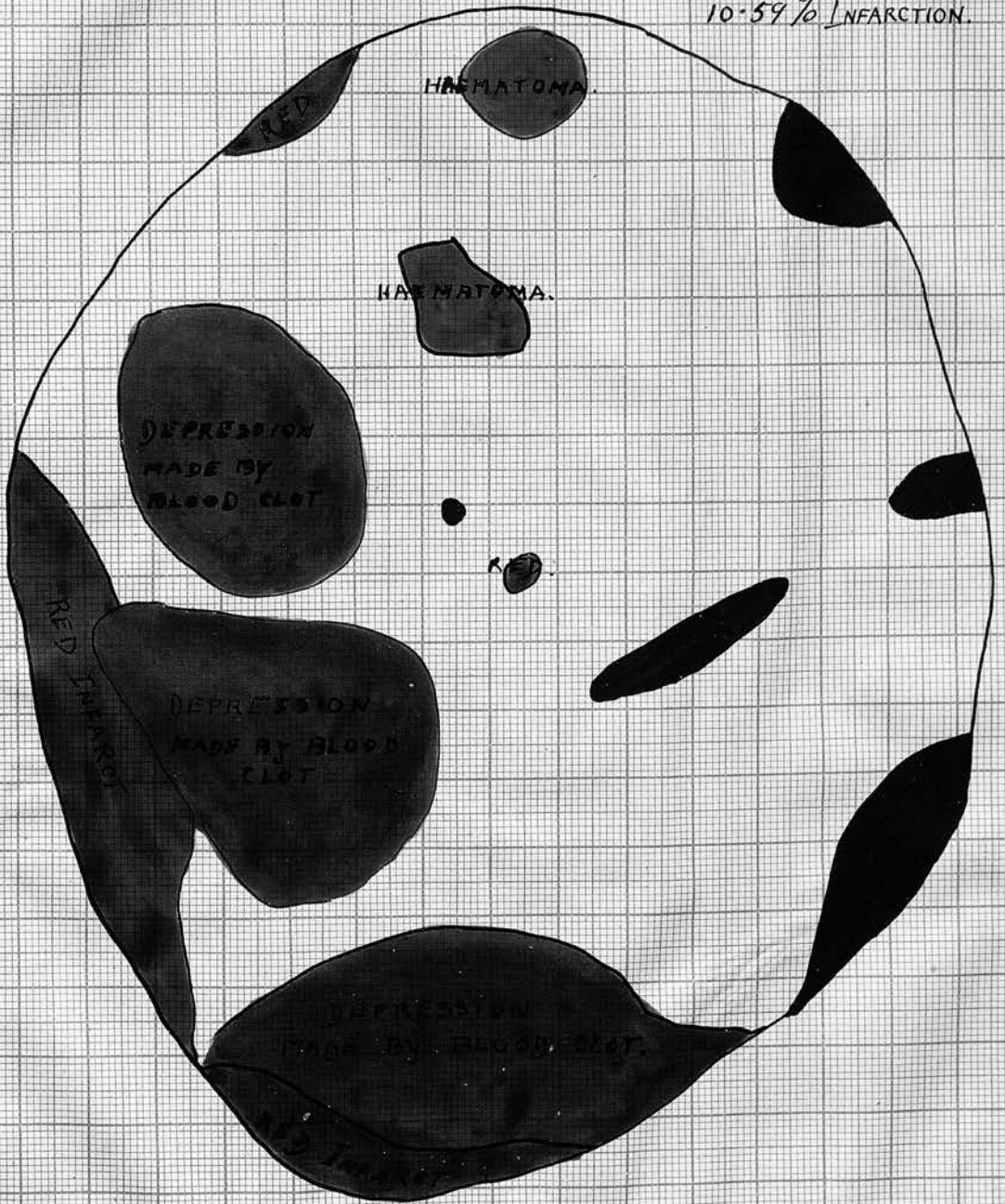
ACCIDENTAL HAEMORRHAGE.
NO INFARCTION.





CONCEALED ACCIDENTAL HAEMORRHAGE.
MATERNAL SURFACE.

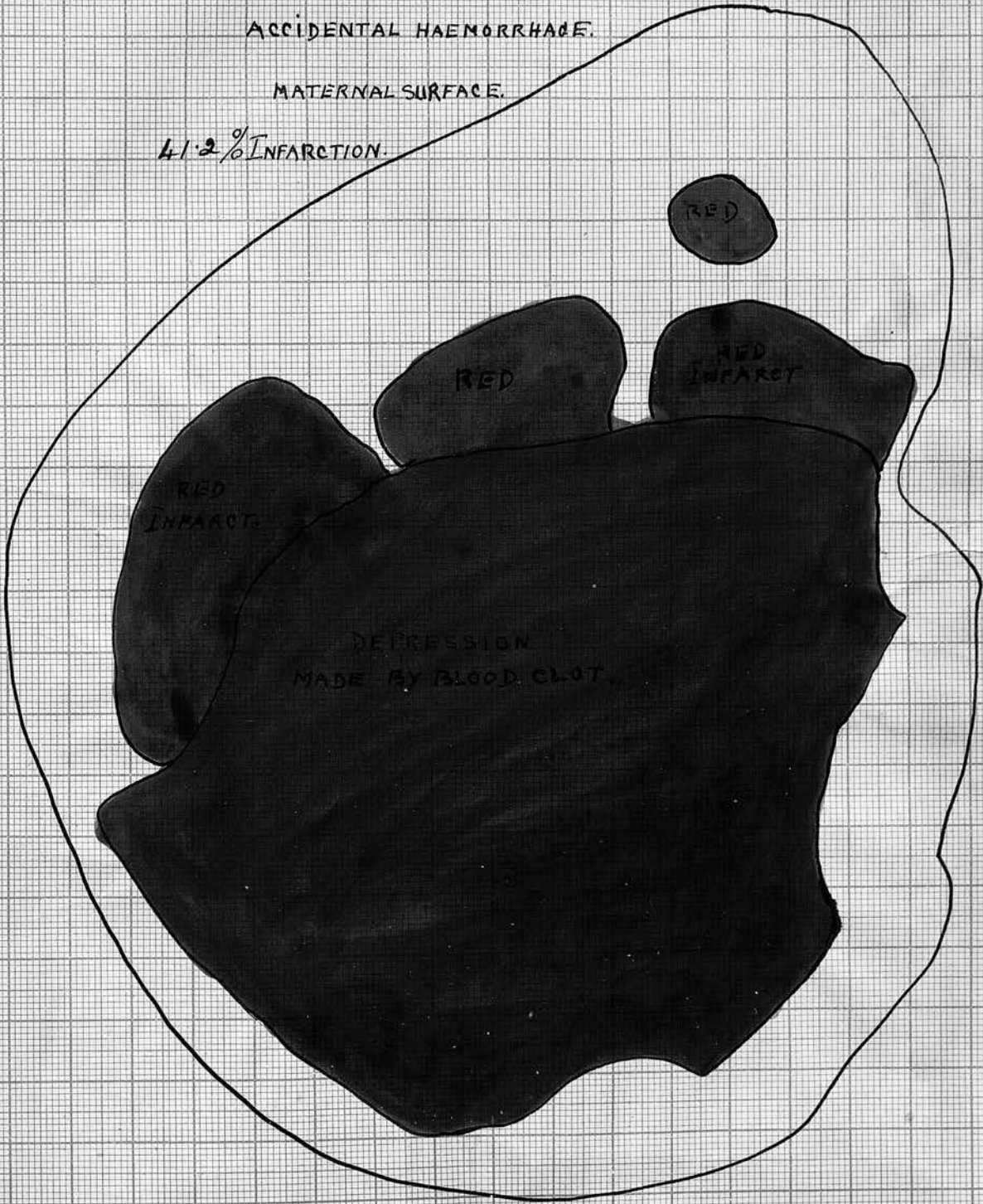
10.59% INFARCTION.



ACCIDENTAL HAEMORRHAGE.

MATERNAL SURFACE.

41.2% INFARCTION.



09.

Summary.

In this series of placentæ from one thousand consecutive deliveries:-

Fibrin deposition was found in 98.6% of all placentæ;

True Infarcts were found in 74.0% of all placentæ.

There were 2761 White Infarcts.

" " 427 Red Infarcts.

∴ 3188 true infarcts in 740 of the placentæ.

There were 250 haematomata in 239 of the placentæ.

There were 136 cases of varying degrees of pre-eclamptic toxæmia in this series. A study of which reveals the following facts:-

1. A mild toxæmia of about one month's duration will result in very little or no infarction of the placenta.

2. A mild toxæmia of long duration will result in massive infarction of the placenta.

3. A severe toxæmia of about one month's duration will result in massive infarction of the placenta.

4. Severe toxæmia does not appear to have a long duration.

There were nine mothers in this series who had Eclampsia. For this small number at least, the eclampsia was not the result of massive infarction of the placenta.

There were 328 cases of varying degrees of hypertension in this series. 72 of these cases had no infarction of the placenta visible to the naked eye. The majority of these 72 had hypertension of less than one/

one month's duration. The study shows a definite increase in the percentage of placental tissue infarcted the longer the duration of the hypertension.

There were 15 cases of accidental haemorrhage in this series. The study of this small group reveals the following facts:-

1. Of twelve cases of accidental haemorrhage uncomplicated by toxæmia only two showed any considerable amount of infarction of the placenta while two showed no placental infarction visible to the naked eye.

11. The three cases of accidental haemorrhage which were complicated by severe pre-eclamptic toxæmia all had massive infarction of the placenta.

Statistical Analysis.Tables and Graphs.

In tables I and II all the numerical results of the survey are shown. The numbers of placentae with the same degree of infarction are shown. These groups are then divided into those that were normal and those that were associated with a series of pathological states.

In table III the same division into groups is followed, the numbers for the whole survey and for those without clinical abnormality being repeated. Also the logarithm of the numbers in each group both for the whole survey and for those without clinical abnormality is shown.

In graph A the number in each group is plotted against the degree of placental infarction.

In graph B the number of patients in each group with no clinical abnormality is similarly plotted.

In graphs C and D this is repeated using for the number of cases a logarithmic scale.

In table IV the numbers in each group for the total survey, with no clinical abnormality, with pre-eclamptic toxæmia, and with hypertension are repeated, also the percentage in each group with pre-eclamptic toxæmia, and with hypertension are shown.

In graph E the number of patients in each group with pre-eclamptic toxæmia is plotted against the degree of placental infarction.

In graph F the percentage number of patients in each group with pre-eclamptic toxæmia is plotted against/

against the degree of placental infarction.

In graph G the number of patients in each group with hypertension is plotted against the degree of placental infarction.

In graph H the percentage number of patients in each group with hypertension is plotted against the degree of placental infarction.

In table V the numbers in each group of a series of pathological states is shown. These numbers are summed for each group and the percentage of the total for the group shown.

In graph J the percentage number of patients with pathology other than pre-eclamptic toxæmia or hypertension is plotted against the degree of placental infarction.

In graph K the distribution of a number of conditions found in the survey, over the infarct range, is shown. There are too few examples of these conditions for them to be considered statistically.

	0-1	1-1	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9	9-10	10-11	11-12	12-13	13-14	14-15	15-16	16-17	17-18	18-19	19-20	20-21	21-22	22-23	23-24	24-25	25-26	26-27	27-28	28-29	29-30	30-31
Percentage of Infarction.	276	43	86	99	98	81	57	47	36	34	32	27	15	16	11	7	4	5	-	6	3	2	1	4	1	1	1	-	-	-	-	-
Total Numbers.	172	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
No Clinical signs, also No Infarction.	-	28	51	47	54	49	30	25	14	14	21	15	5	10	2	3	-	1	-	2	-	-	-	-	-	-	-	-	-	-	-	-
No Clinical signs but Infarction.	2	1	-	-	-	1	1	-	-	1	-	-	-	-	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Eclampsia.	21	7	8	16	13	8	11	7	3	9	4	5	2	3	2	1	-	2	-	2	1	1	1	1	1	1	-	-	-	-	-	-
Pre-eclamptic Toxaemia.	72	14	23	39	27	27	11	16	16	17	9	10	8	6	7	3	3	4	-	3	2	1	1	1	1	1	-	-	-	-	-	-
Hypertension.	8	0	4	2	1	2	1	-	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pyelitis.	17	2	5	7	5	4	2	2	4	4	-	2	3	3	1	1	1	1	1	1	2	-	-	1	-	-	-	-	-	-	-	-
Ante-partum Haemorrhage.	3	-	-	3	-	1	-	-	-	-	-	2	1	1	-	-	1	-	-	1	-	-	-	-	-	-	-	-	-	-	-	-
Accidental Haemorrhage.																																

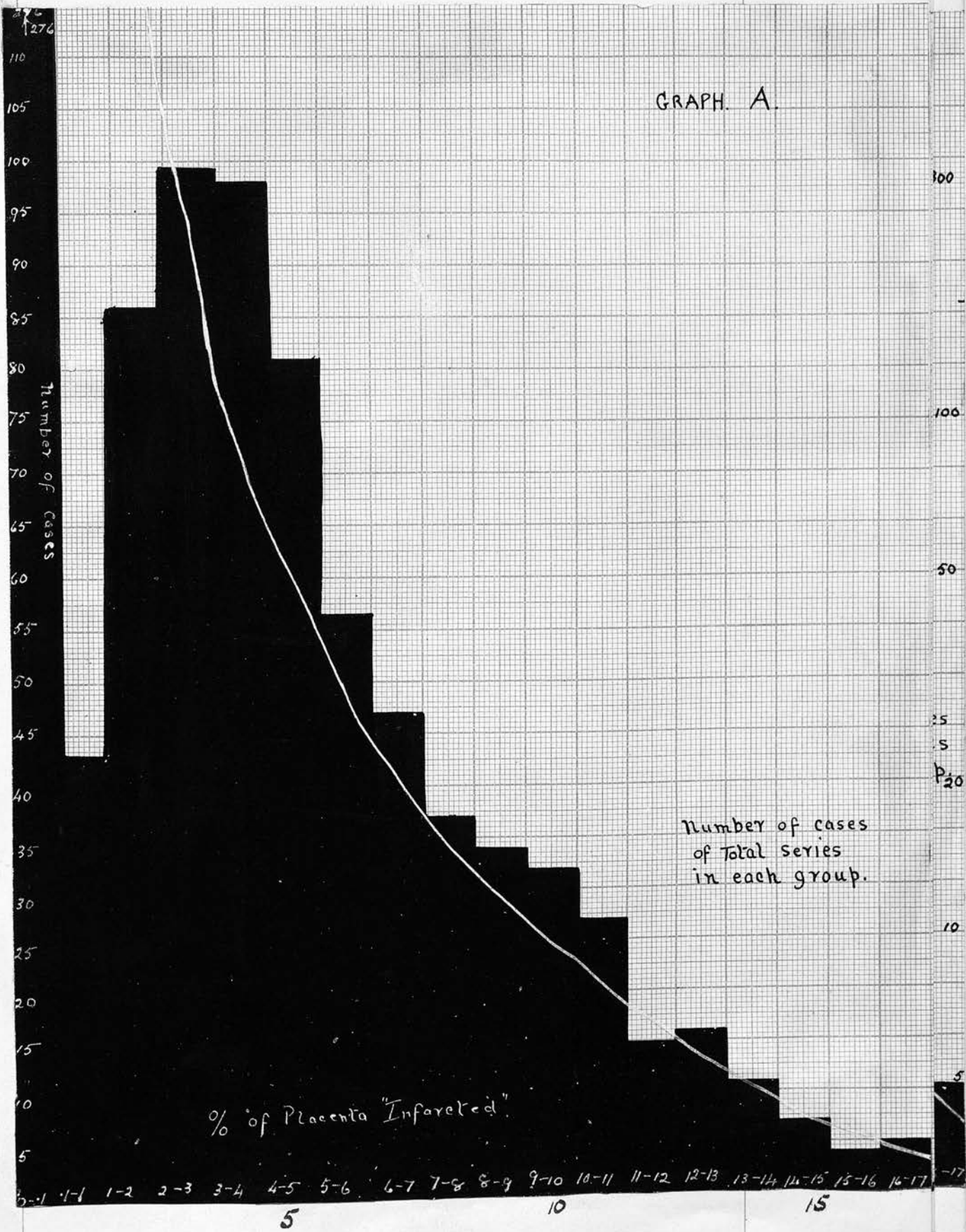
Table I.

Percentage of Infarction.	31-32	32-33	33-34	34-35	35-36	36-37	37-38	38-39	39-40	40-41	41-42	42-43	43-44	44-45	45-46	46-47	47-48	48-49	49-50	50-51	51-52	52-53	53-54	54-55	55-56	56-57	57-58	58-59	59-60	60-61	61-62	
Total Numbers.	-	-	-	-	-	-	/	-	-	-	/	-	-	-	-	-	-	/	-	-	/	-	-	-	-	-	-	-	-	-	2	/
No Clinical signs also	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
No Infarction.	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
No Clinical signs but Infarction.	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Eclampsia.	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pre-eclamptic Toxaemia.	-	-	-	-	-	-	-	-	-	-	/	-	-	-	-	-	-	/	-	-	-	-	-	-	-	-	-	-	-	2	/	-
Hypertension.	-	-	-	-	-	-	/	-	-	-	/	-	-	-	-	-	-	/	-	-	-	-	-	-	-	-	-	-	-	2	/	-
Pyelitis.	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	/	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Ante-partum Haemorrhage.	-	-	-	-	-	-	-	-	-	-	/	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	/	-
Accidental Haemorrhage.	-	-	-	-	-	-	-	-	-	-	/	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	/	-

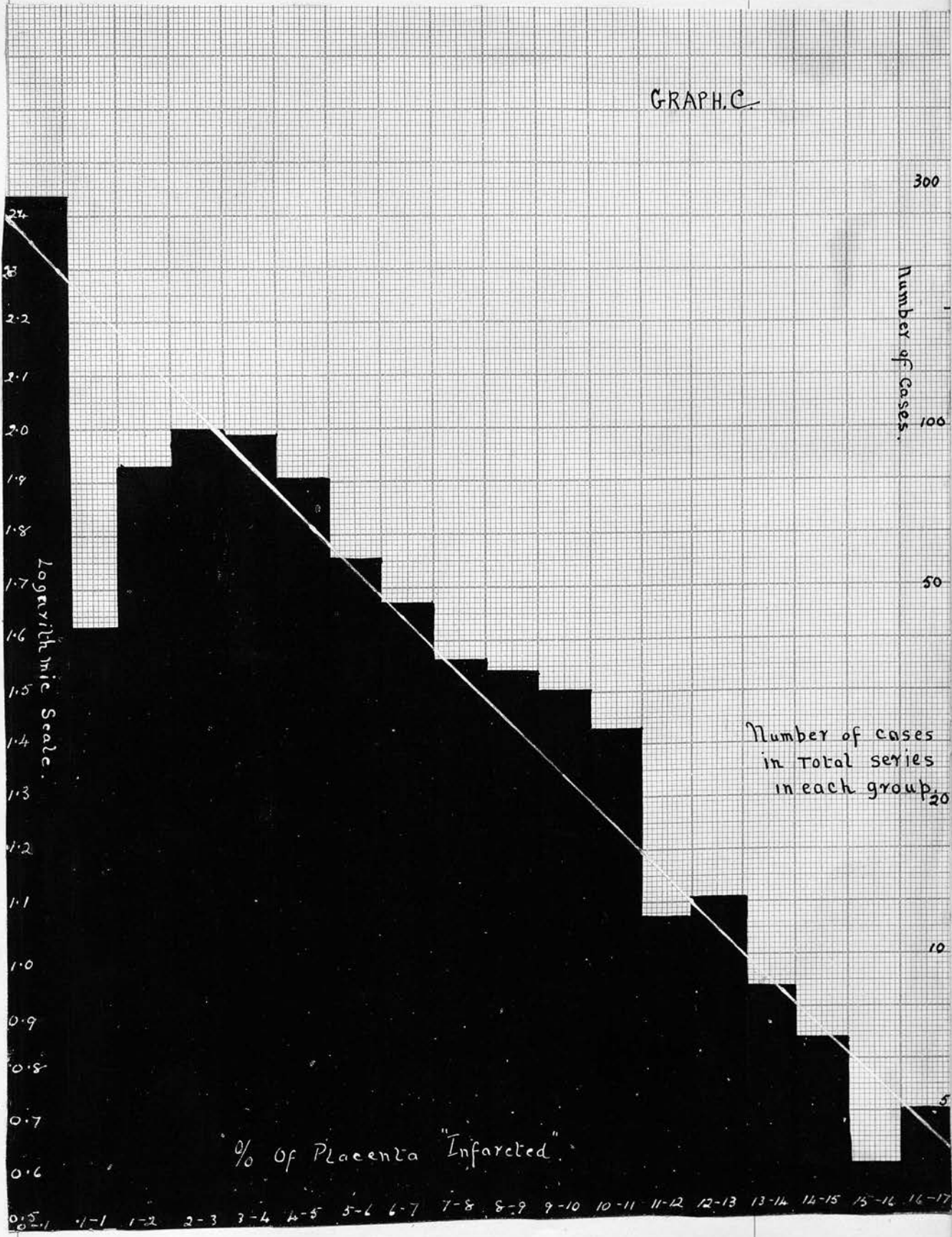
Table II

Percentage of Erythrocytes	0-1	1-1	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9	9-10	10-11	11-12	12-13	13-14	14-15	15-16	16-17	17-18
TOTALS.	276	43	86	99	98	81	57	47	36	34	32	27	15	16	11	7	4	5	0
Lot of Totals.	2.4409	1.6386	1.9245	1.9986	1.9922	1.9086	1.7539	1.6721	1.5583	1.5313	1.5051	1.4344	1.1761	1.2041	1.0442	0.8469	0.6021	0.8996	—
Group Clinical signs Nil.	172	28	51	47	54	49	30	25	14	14	21	15	5	10	2	3	0	1	0
Lot of group Clinical signs Nil.	2.2355	1.4472	1.7076	1.6721	1.7324	1.6902	1.4771	1.3879	1.1461	1.1461	1.3222	1.1761	0.6998	1.000	0.9000	0.4171	—	—	—

Table III



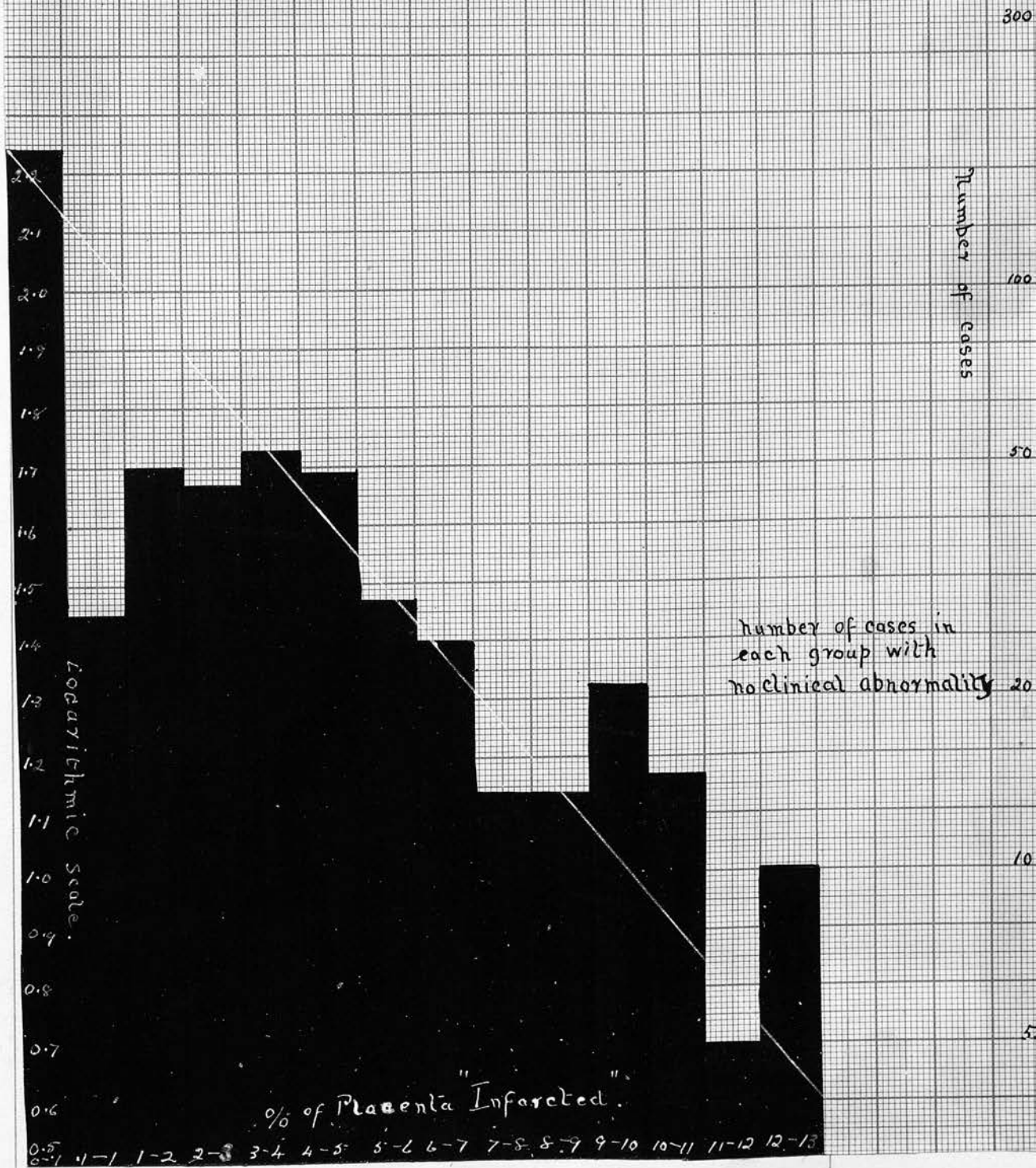
GRAPH.C



Percentage of Infarction.	0-1	1-1	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9	9-10	10-11	11-12	12-13	13-14	14-15	15-16	16-17	17-18
Totals.	276	43	86	99	98	81	57	47	36	34	32	27	15	16	11	7	4	5	—
Clinical signs nil.	172	28	51	47	54	49	30	25	14	14	21	15	5	10	2	3	—	1	—
Pre-eclamptic Toxaemia.	21	7	8	16	13	8	11	7	3	9	4	5	2	3	2	1	—	2	—
% Pre-eclamptic Toxaemia.	7.6%	16%	9.4%	16%	13%	10%	19%	15%	8.6%	26%	13%	19%	13%	19%	18%	—	—	—	—
Hypertension.	72	14	23	39	27	27	11	16	16	17	9	10	8	6	7	3	3	4	—
% of Hypertension.	26%	33%	27%	39%	28%	33%	19%	34%	44%	50%	28%	37%	53%	37%	64%	43%	—	—	—

Table IV.

GRAPH. D.



GRAPH. E.

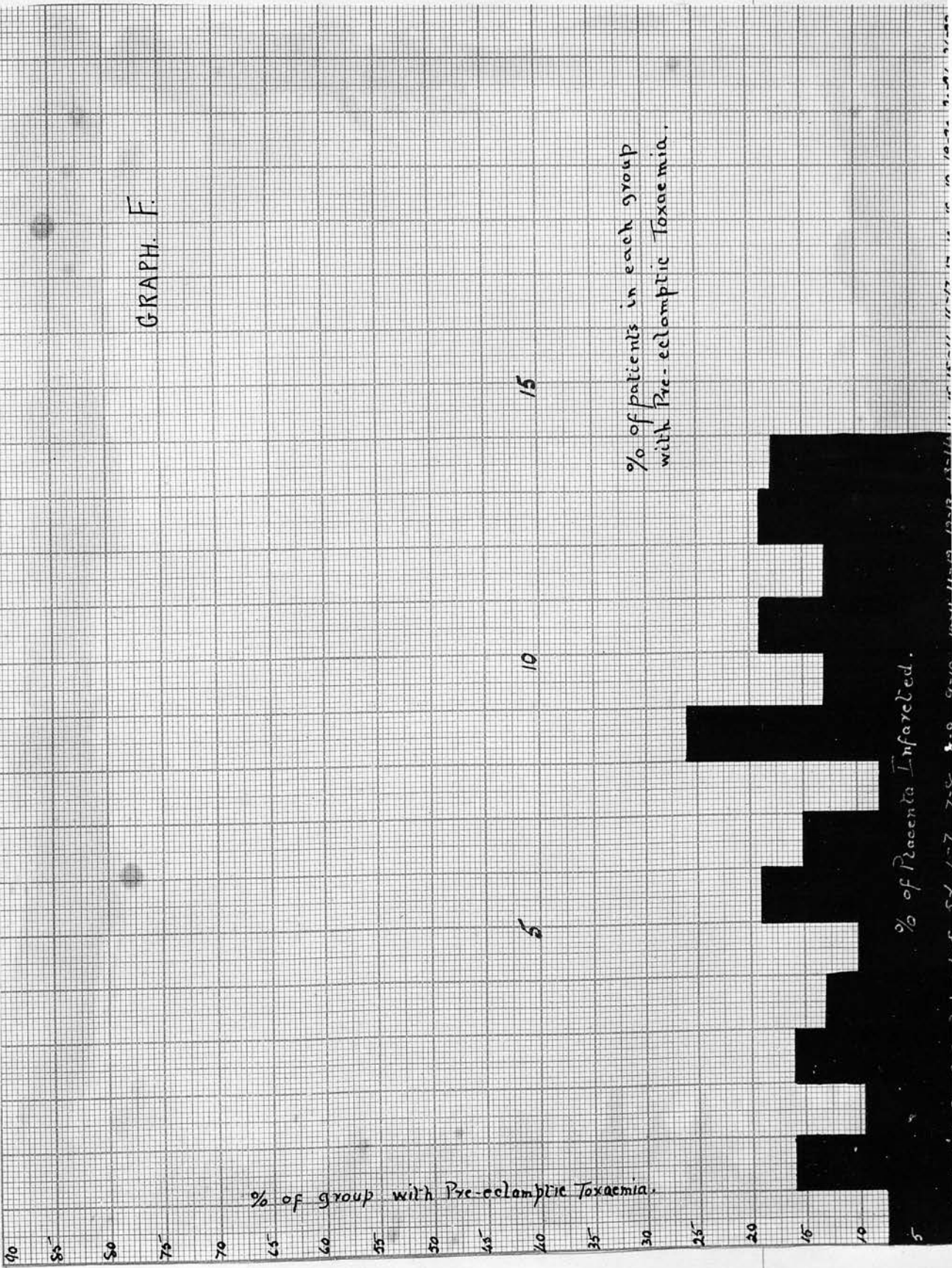
Number of patients with
Pre-eclamptic Toxaemia
in each Infarct group.

Number of patients with pre-eclamptic Toxaemia.

50
45
40
35
30
25
20
15
10
5

% of Placenta Infarcted.

GRAPH. F.



% of group with Pre-eclampsia Toxaemia.

% of patients in each group with Pre-eclampsia Toxaemia.

% of Placenta Infarcted.

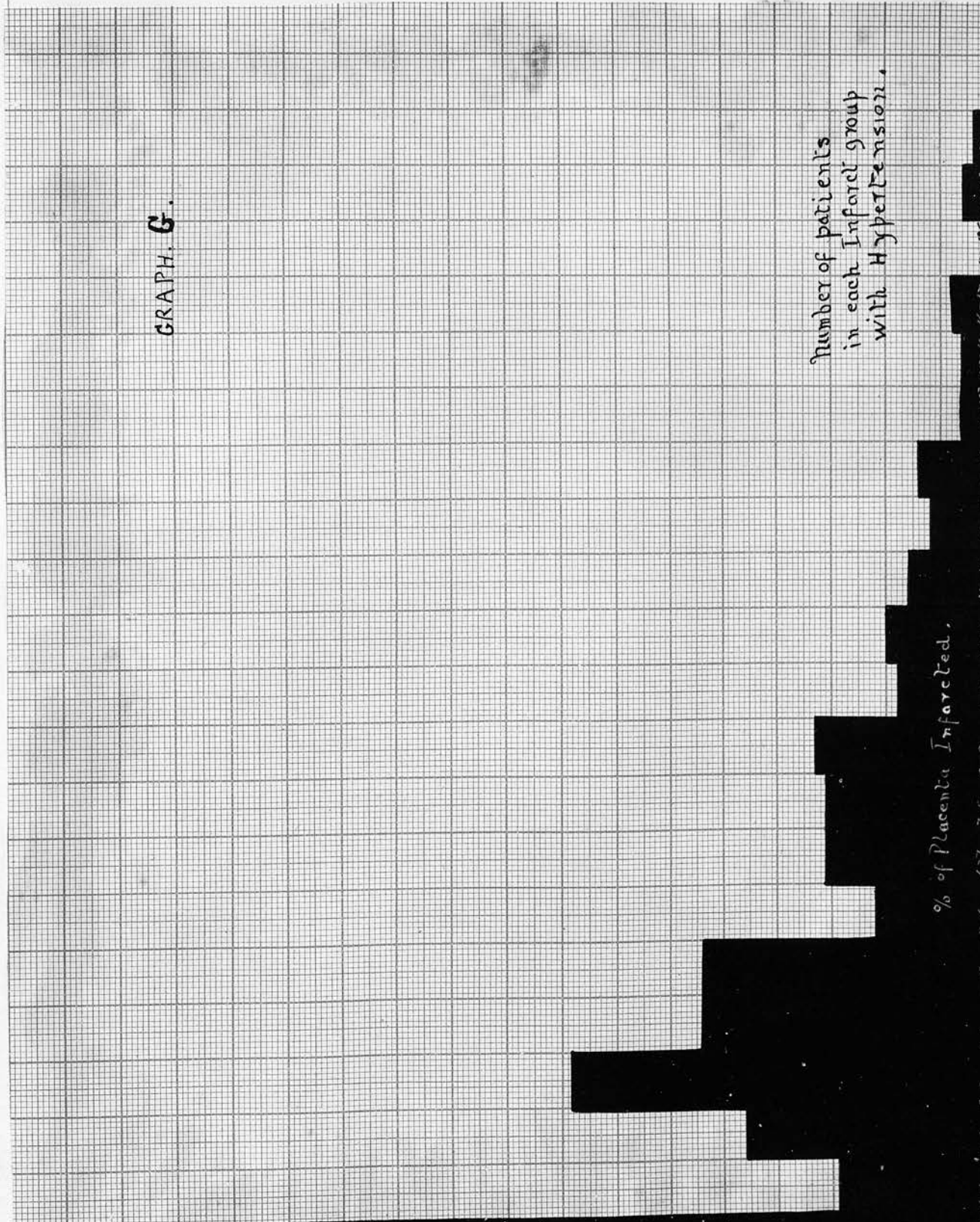
GRAPH. G.

Number of patients
in each Infarct group
with Hypertension.

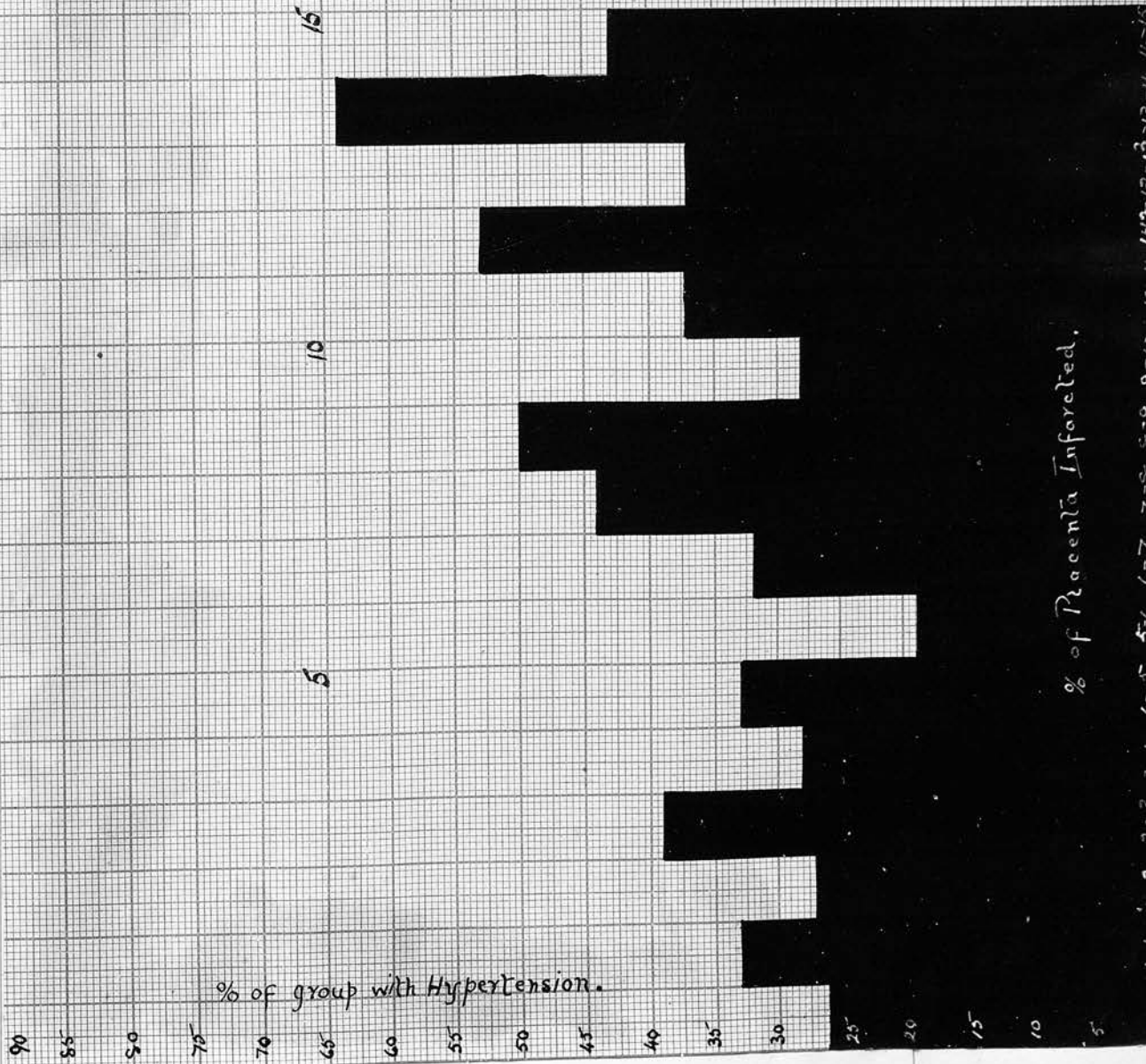
% of Placenta Infarcted.

65
50
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5

number of cases.



GRAPH. H.



% of Patients Infarcted.

Percentage of Infarction.	0-1	1-1	1-2	2-3	3-4	4-5	5-6	6-7	7-8	8-9	9-10	10-11	11-12	12-13	13-14	14-15	15-16
Pyelitis.	8	0	4	2	1	2	1	0	0	1	0	0	0	0	1	0	—
Diabetes.	1	0	0	2	1	0	0	0	0	0	0	0	0	0	0	0	—
Syphilis.	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	—
Gonorrhoea.	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	—
Carcinoma of Cervix.	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	—
Epilepsy.	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	—
Asthma.	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	—
Tuberculosis.	1	0	0	0	2	0	1	1	0	0	0	0	0	0	0	0	—
Renal Glycosuria.	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	—
Cardiac.	7	1	2	1	3	0	1	2	0	1	0	0	0	0	1	0	—
Thyrotoxicosis.	1	0	0	1	0	0	0	0	2	0	0	0	0	0	0	0	—
Total of Pathological Group.	20	1	3	6	7	3	3	4	2	2	0	1	0	0	2	0	—
Percentage of Total.	7.3%	2.3%	3.5%	6.1%	7.2%	3.7%	5.3%	5.3%	5.6%	5.9%	0%	3.7%	0%	0%	1.8%	0%	—

Table V.

GRAPH. J.

% of group

30
25
20
15
10
5

% of patients with pathology other than
Toxaemia of Pregnancy.

% of Patients Infected.

10-11 11-12 12-13 13-14 14-15 15-16 16-17 17-18 18-19 19-20 20-21 21-22

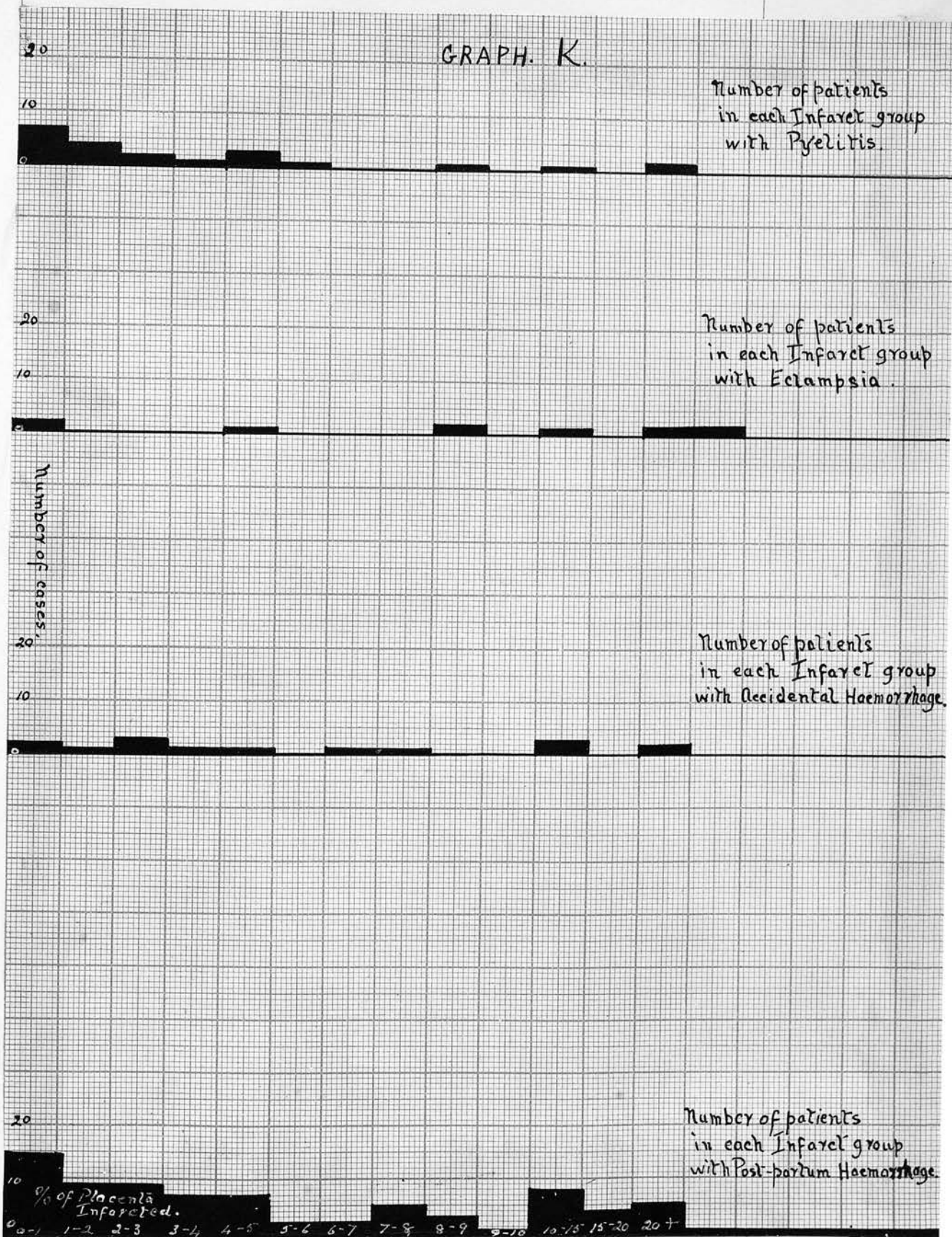
GRAPH. K.

Number of patients
in each Infaret group
with Pyelitis.

Number of patients
in each Infaret group
with Eclampsia.

Number of patients
in each Infaret group
with Accidental Haemorrhage.

Number of patients
in each Infaret group
with Post-partum Haemorrhage.



Conclusions.

Either a severe toxæmia of over one month's duration, or a mild toxæmia of a much longer duration, will result in massive infarction of the placenta.

It is possible to get massive infarction of the placenta without clinical signs or symptoms of toxæmia.

It is possible to get "Eclampsia" without infarction of the placenta.

The longer the duration of the hypertension rather than the height of the mercury determines the degree of infarction of the placenta.

That accidental hæmorrhage uncomplicated by toxæmia does not cause massive infarction of the placenta.

That accidental hæmorrhage when complicated by severe pre-eclamptic toxæmia does cause massive infarction of the placenta.

Conclusions drawn from the "Statistical Analysis".

In this survey there were only sufficient examples for placentæ with less than 15.0% of their tissue infarcted to be considered statistically.

In this series the frequency distribution of degree of infarction was regular, such that the relation between degree of infarction and logarithm frequency could be represented by a straight line (see graphs A and C.)

This may begin to explain the cause of infarction.

The same kind of relation was found in a series of cases with no clinical abnormality, selected from the main/

main series of cases; but in this graph there was more scatter (see graphs B and D).

In the whole series there were 343 placentae with more than 1.0% of their tissue "infarcted". While there were no clinical signs or symptoms of toxæmia in the mothers, 38 of these placentae had more than 10.0% of their tissue "infarcted". It seems probable that these infarcts were caused by factors independent of hypertension, or of toxæmia of pregnancy, at least as far as this is recognised clinically. (See graph D)

Pre-eclamptic toxæmia was found with all degrees of placental infarction within the limits of this survey, (except in 15.0% and 16.0% - this is thought to be a sampling error).

There were 21 cases of pre-eclamptic toxæmia in which no placental infarction was observed.

The percentage of each infarct group with clinical signs or symptoms of pre-eclamptic toxæmia appears to show some correlation with the degree of placental infarction. (See graphs E and F.)

Hypertension was associated with all degrees of placental infarction.

There were 72 cases with hypertension in which no placental infarction was observed.

Infarction of the placenta appears to be positively correlated with hypertension. (See graphs G and H.)

Thus it seems that both pre-eclamptic toxæmia and hypertension are correlated with placental infarction more often than would be expected if the association/

association was only due to coincidence, but the association is not absolute.

It is possible to get eclampsia without having infarction of the placenta. (See graph diagram of placenta.)

It is possible to get massive infarction of the placenta without clinical toxæmia. (See graph diagram of placenta.)

Foetal Surface.



A placenta showing a Chorionic Cyst.

Microphotographs.

No. 1. Part of an old (white) infarct. Magnification X 100. Showing chorionic villi densely packed together, degenerated and poorly staining; some normal placental tissue is seen. This case showed no clinical abnormality.

No. 2. This shows large thrombosed vessel surrounded by densely packed chorionic villi; a little normal placental tissue is seen. Magnification X 100. This case showed no clinical abnormality.

No. 3. Part of a recent (red) infarct. Magnification X 100. Showing disintegration of the infarct; in the lower right-hand corner the chorionic villi are densely packed together. From a case of accidental haemorrhage. B.P. 200/140. Alb. +++.

No. 4. Part of an old (white) infarct. Magnification X 100. Chorionic villi densely packed together. Markedly engorged bloodvessels well seen. From a case of mild hypertension. B.P. 132/78. Alb. negative.

No. 5. Part of an old (white) infarct. Magnification X 100. Showing clearly fibrin deposition. Surrounding chorionic villi densely packed together; clubbing of the villi. From a case of hypertension. B.P. 140/80. Alb. negative.

No. 6. Part of an old (white) infarct. Magnification X 100. Showing a laminated appearance. From a case of mild hypertension. B.P. 135/85. Alb. negative.

No. 7. Part of an old (white) infarct. Magnification X 100. Showing marked infarction. From a case of mild hypertension. B.P. 130/85. Alb. negative.

No. 8/

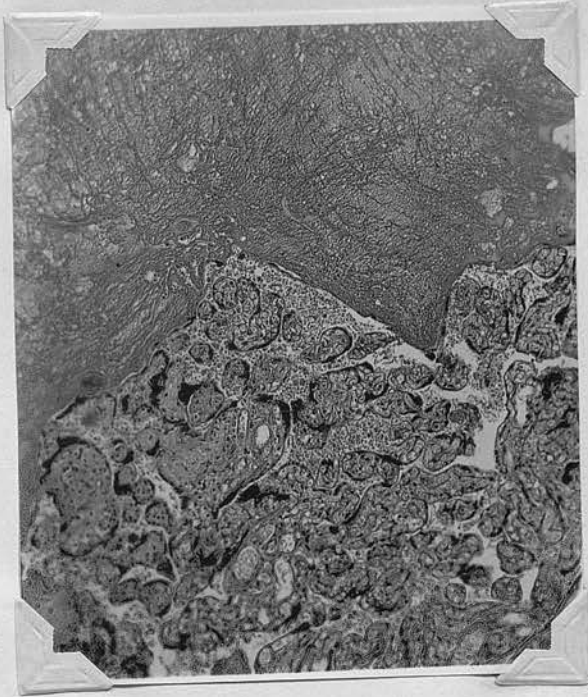
No. 8. Part of a haematoma. Low power. Magnification
X 65. Showing packed chorionic villi above the
haematoma. From a case of antepartum haemorrhage.
B.P. 120/70. Alb. negative.

No. 9. Part of an old (white) infarct. Magnification
X 100. Showing infarction with marked degeneration.
From a case with no signs of clinical abnormality.

No. 10. Part of an old (white) infarct. Magnification
X 100. Showing clearly marked infarction around
three bloodvessels. From a case with no signs of
clinical abnormality.

Microphotographs.

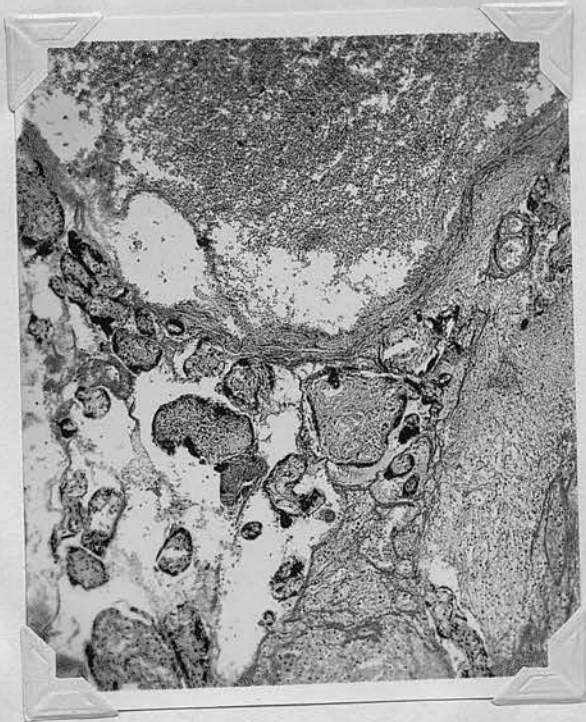
(For descriptions see pages 92 and 93.)



I



II



III



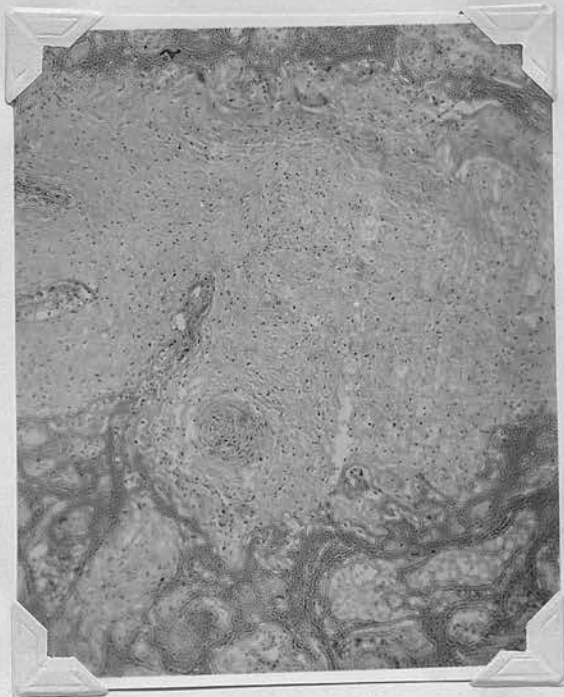
IV



V



VI



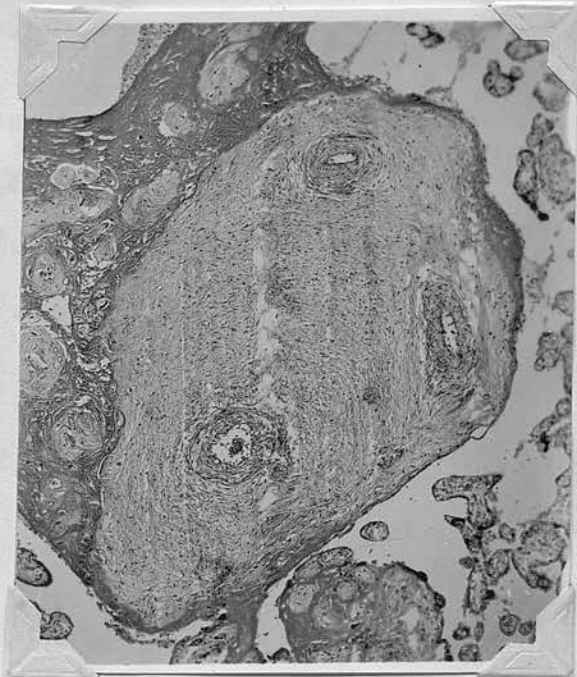
VII



VIII



|X|



|X|

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