Review

TOXAEMIAS OF PREGNANCY

Review

by

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Hypertension is frequently observed during pregnancy; whether it is incidental to pregnancy or an unmasked inherent tendency, is yet an unsolved riddle. The obstetrician who observes the condition is often not certain as to the order of precedence. Prolonged observation and investigations are required to settle whether hypertension was the result of pregnancy or not. Hence, from the clinical standpoint it is best to group these conditions together under the descriptive heading of Toxaemias of Pregnancy.

Classification of Toxaemias of Pregnancy:

Under this heading three common conditions are included;

(1) Specific pre-eclampsia and eclampsia of pregnancy.

2) Essential hypertension complicating pregnancy.

(3) Chronic nephritis complicating pregnancy.

Aetiology of Pre-eclamptic Toxaemia

Various attempts have been made to explain the entire symptom-complex of hypertension, proteinuria and oedema complicating pregnancy on the basis of a single disturbance like vascular spasm, electrolyte imbalance, hormonal disturbance or nutritional deficiency. However, the evidences set forth in support of these views have often been conflicting and in total disagreement. The anatomical lesions in the liver and the kidney cannot be ascribed to hypertension or an underlying vascular spasm. the oedema is often an exaggeration of a process commonly observed in almost a third or more of the pregnancy population. Finally, the whole disturbance tends to disappear with parturition, an event that may be attributed most probably to the discharge of the placenta.

The following factors predispose to pre-eclampsia, primigravidity, dystocia-dystrophia-syndrome, hydramnios, diabetes, multiple pregnancy, molar pregnancy, nutritional deficiency, essential hypertension and chronic nephritis.

Taken as a whole these factors suggest that the occurrence of toxaemia is dependent upon two factors, the sensitivity of the vascular system and the conditions prevailing in the uterus. So far as the latter is concerned, the oft repeated observation of toxaemia complicating

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hydatidiform mole, a condition in which the foetus is often absent, suggests the trophoblastic tissue and its derivative, the placenta and decidua, as the locus of the primary disturbance. A similar conclusion absolving the foetus of playing a role in the causation of pregnancy toxaemia has been arrived at on the basis of the works of Browne and Dodds (1936), Woodbury *et al,* (1938) and Dexter and Weiss (1941). These workers compared the blood pressures of infants born of toxaemic and normal mothers and they were unable to demonstrate any significant difference in the two groups.

Young (1914) drew attention to the association of placental infarcts and toxaemia, and suggested this to be the site from which toxins were liberated. Smith and Smith (1948) postulated that the ischaemic placenta in toxaemic women liberated 'menotoxin'. The hypothesis that ischaemia of the gravid uterus is the essential cause of pregnancy toxaemia has been particularly espoused by Bastiaanse and Mastboom (1950), Ogden *et al* (1950). Bastiaanse and co-workers (1950) have experimentally induced hypertension by constricting the uterine arteries. The association between toxaemia and reduction in choriodecidual circulation is further supported by isotope transfer studies by Browne and Veale (1953), Dixon *et al* (1963), and others. Franklin and Sophian (1952) believe that the stretch resisting impulses from the uterus reflexly induce renal ischaemia and cause pre-eclampsia. Mukherjee (1961) has experimentally shown that the bladder overdistension in animals also induces a similar renal response. Hunter and Howard (1960) have more recently demonstrated a toxic substance 'hysterotonin' in the decidua and amniotic fluid of ischaemic uteri of toxaemic women. They explain that the improvement in the clinical condition after parturition is the result of expulsion of the offending liquor, placenta and decidua.

Dietetic factors have also been incriminated in the causation of pregnancy toxaemia from time to time. King and Ride (1945) attributed pre-eclampsia to the B-complex deficiency prevalent amongst the poor Chinese population of Hong Kong. Whiteacre *et al* (1947), on the basis of wide experience in the orient and the United States, suggested that dietary deficiency of first class proteins, vitamins and minerals was responsible for the toxaemic state. Theobald (1937) was convinced in a controlled clinical trial, that vitamins and mineral supplements during the antenatal period helped to lower the incidence of pregnancy toxaemia.

Hormones have been blamed as causative factors. Anselmino and Hoffman (1936) pointed to a posterior pituitary substance as an aetiological factor; however, Browne (1944) on reviewing further work on the subject was unable to confirm the earlier view. Ham and Landis (1942) showed the presence of an antidiuretic substance occurring with higher frequency in the placenta of toxaemic women. Brown, *et al* (1966) have measured the plasma concentrations of renin, angiotensin and aldosterone amongst normal gravid and toxaemic subjects. They

have not noted any significant difference. Smith and Smith (1940) reported abnormally raised chorionic gonadotrophin values in toxaemic women, and De Watteville (1951) demonstrated lowered oestriol and pregnanediol excretion values, thus proving a disturbed hormonal metabolism in toxaemic women; however, no cause and effect relationship can be established.

Lastly, Sims (1965) has suggested auto-immune mechanism as a possible underlying factor. More work in this direction is required to explore this field.

Pathology

The pathologic changes of pregnancy toxaemia can be conveniently described under the following three headings:

1. *Pathological Anatomy:* Autopsy studies in toxaemic subjects commonly reveal changes in the liver, kidneys, brain, lungs, heart and the uterus.

(a) *Liver:* The liver appears enlarged and shows subcapsular haemorrhages. On cut section, mottled areas of haemorrhages are clearly visible. On microscopic examination, areas of periportal necrosis, associated with extensive thrombosis in the small vessels of the connective tissue, are evident. Theobald (1932) and Davidson (1931) are of the opinion that peripheral necrosis is not a constant finding. Acosta-Sison (1931), Way (1941) and Bell (1926) have shown that in severely affected women widespread hepatic necrosis may occur. Dhawan and Dhall (1964) showed that in 50% of women suffering from severe pre-eclampsia, there was no hepatic abnormality, whereas in 20% there was fatty change, and in 10% the liver showed perisinusoidal oedema.

(b) *Kidneys:* The typical kidney lesion is characterised by (i) swelling of the endothelial cells of the basement membrane, (ii) deposition of amorphous material against the basement membrane and (iii) cellular increase in between the capillary loops. Rarely, bilateral cortical necrosis may occur.

(c) *Brain:* The brain at autopsy shows changes of oedema, hyperaemia, anaemia, thrombosis and haemorrhage. Cut section reveals petecheial haemorrhages; rarely it may show massive haemorrhage.

(d) *Heart:* This organ is involved to a varying degree in cases of severe pre-eclampsia; the myocardium shows cloudy or fatty degeneration according to Schmorl (1893). In a few cases he also showed haemorrhage and necrosis in the myocardium. Sheehan (1950) described sub-endocardial haemorrhage on the left side of the interventricular septum in a majority of women dying of eclampsia.

(e) *Uterus:* In antepartum deaths, the uterine musculature appears oedematous, the placenta shows infarcts and a retroplacental clot may be present. In post-partum cases a flabby uterus showing cloudy degeneration is obvious. In severely affected women with accidental haemorrhage, the serous coat will show mottling due to haemorrhages, described as the Couvelaire uterus.

(f) *Lungs:* Varying degrees of pulmonary oedema are usual.

II. *Pathologic Physiology:*

Vasospasm is the principal underlying change in the pathophysiology of acute toxaemia. Volhard (1934) first advanced this concept. Hinselman (1924) observed changes of vasospasm in the smaller blood vessels of the nail bed. Landesman *et al* (1954) described marked arteriolar vasoconstriction in severely affected women. Mylius (1929), Wagner (1933), and Hallum (1936) described vasospasm on fundoscopic examination. Finnerty (1954) states that if vasospasm persists for long, permanent sclerotic changes are induced. Agarwal *et al* (1954), employing ophthalmodynamometry, concluded that the diastolic pressure in the retinal vessels rises early in the course of pre-eclampsia. Kishore and Tandon (1965) state that retinal artery changes run parallel with the clinical severity of the disease.

Renal ischaemia is the cause of proteinuria. Chesley *et al* (1948) demonstrated renal ischaemia by employing the cold pressor test.

Munell and Taylor (1947) were unable to demonstrate any remarkable changes in the hepatic blood flow in women suffering from severe pre-eclampsia. So also McCall (1953) found normal cerebral blood flow in pre-eclampsia and eclampsia.

Burt (1951) reported an increase in the blood flow to the skin and muscles of the extremities.

Assali (1954) and Browne and Veall (1953) showed a reduction in the blood flow to the choriodecidual space, and Moore *et al* (1957) observed a similar reduction of blood supply to the uterine myometrium.

III. *Pathologic Biochemistry:*

The major biochemical change in pregnancy toxaemia is a disturbance of salt and water metabolism. On the basis of classical balance experiments, it has been widely assumed that toxaemic women retain an excess of salt. However, Gray and Plentl (1954), Dieckmann *et al* (1956) and others, using radioactive Na^{24} tracer techniques, have not been able to demonstrate any increase in the total exchangeable sodium space. MacGillivray and Buchanan (1958) are of the opinion that water retention, rather than sodium retention, is the important abnormality in pre-eclampsia. Gray and Plentl (1954) are also of a similar opinion. These authors have demonstrated that water retention precedes clinical oedema.

Dieckmann and Mickel (1937) have demonstrated poor salt tolerance in toxaemic subjects, and Harding and Van Wyck (1938) believe that a high salt intake at a critical time in toxaemic women is likely to cause proteinuria, increase in hypertension and even fits.

Chesley (1944) points out that toxaemic women excrete large amounts of sodium in the puerperium, and therefore he concludes that these women retain excess of salt during pregnancy.

Severe pre-eclampsia and eclampsia is associated with an aberrant protein metabolism; however, these changes are seldom associated with any significant sodium retention. The values of blood urea, uric acid, non-protein nitrogen and serum protein fractions have been studied by

various authors; the results of their studies reveal significant differences.

Kishore and Tandon (1965) compared the average values of blood urea, non-protein nitrogen and uric acid in non-pregnant, normal pregnant and toxaemic women. Their findings reveal that blood non-protein nitrogen does not significantly alter in pregnancy and during toxaemia. The blood urea value drops in pregnancy and is elevated in the toxaemic state. The blood uric acid shows a significant rise, and this rise runs parallel with the increase in the clinical severity of the disease and corresponds to the changes in the eye grounds. Juvale and Gokhale (1964) studied the urea clearance values in the normal pregnant and toxaemic women; they were unable to demonstrate any significant difference. Chesley and Chesley (1939) attribute the rise in blood uric acid in toxaemic subjects to a diminution of renal uric acid clearance values; these authors are of the opinion that hepatic damage is in no way related to the rise in uric acid levels.

The serum protein levels and the inter-relations between the various fractions have been studied extensively. Mack (1951) observed a lowering in the mean total plasma proteins, albumin, beta and gamma globulins amongst toxaemic subjects. The other globulin fractions tend to increase. Purandare *et al* (1954) studied blood protein values in Indian women; they observed that a reduction of albumin fraction was associated with a slight increase in the globulin in severely affected women only. Menon *et al* (1957) observed a marked drop in the albumin fraction, but the alterations in values of alpha$_1$, alpha$_2$ and beta globulins were not statistically significant, though the lowering of gamma globulin values was significant. Purandare and Agashe (1958) also studied serum protein fractions and they observed a rise in alpha$_1$, alpha$_2$ and beta globulins in pre-eclampsia which is not observed in eclampsia, and a significant increase in gamma globulins in eclampsia. Kulkarni *et al* (1968) have also recorded a similar fall in total proteins and a significant drop in serum albumin in severely toxaemic women.

Dieckmann and Pottinger (1956), Purandare and Agashe (1955) and Kaur and Dhall (1965) have all reported a rise in fibrinogen values over the normal values observed in pregnancy The rise is higher in eclampsia as compared to pre-eclampsia.

Santhanagopalan *et al* (1965) reported elevated values of the blood enzymes SGOT and SGPT in toxaemic women. Dass and Bhagwanani (1964) also demonstrated increase in serum transaminase values in toxaemia, which they attribute to hepatic damage. Kirpalani and Jeacock *et al* (1962) showed elevated serum iso-citric dehydrogenase values in severe toxaemias. Sunandabai (1967) also observed raised serum iso-citric dehydrogenase values in severely affected toxaemic women.

Cassmer (1959), Marius and du-Toit (1965), Wakhaloo and Dhall (1966) and Varangot *et al* (1965) have all shown lowered oestriol excretion values in toxaemic women. They attribute this to placental dysfunction.

Clinical Features

The characteristic signs and symptoms are discussed in the following paragraphs:

1. *Raised blood pressure:* This may be the first sign to be observed on routine prenatal check-up after mid-pregnancy. Occurrence of hypertension before mid-pregnancy is a sign of essential hypertension while pre-eclampsia commonly supervenes later. The rise in pressure commonly develops slowly after the 32nd week, but it may ocur earlier and rise rapidly over a period of a few days. The accepted standard of hypertension is a rise of pressure exceeding 140/90 mm.Hg. Increased diastolic pressure over 90 mm. Hg. is more significant than a rise in systolic pressure. Even a lower figure of 130/90 mm.Hg. in a woman who has been consistently having low pressures like 115/60-70 is of significance as a warning sign. The cause of hypertension is vasospasm. Some symptoms depend upon the sites of vasospasm, e.g. in the kidneys albuminuria, in the brain eclamptic fit; in the uterus abruptio placentae; in the eyes diminished vision and haemorrhages; in the liver hepatic damage and insufficiency.

2. *Oedema:* Postural oedema of the legs and feet is common in normal pregnancy, but oedema is not noticeable in other parts of the body. As a result of altered salt and water metabolism in the toxaemic state, these women tend to retain fluid. Oedema may sometimes be the first sign to appear. Weight gain frequently precedes the onset of overt oedema; the practice of routinely weighing the patient at every prenatal visit often gives the first clue that the patient is retaining too much fluid and thus incipient oedema can be suspected before manifest signs appear. Toxaemic oedema usually involves the ankles and the feet first; the patient may notice stiffness in movements of her fingers in the morning. Some women notice a tightening of the wedding ring; puffy face and eyelids are observed in moderately severe cases. Sometimes, vulval oedema can be pronounced and may interfere with labour. The exact cause of oedema is not known, but increased orthostatic pressure, increased sodium and fluid retention as a result of increased endogenous steroid levels, increased capillary permeability and lowered osmotic pressure of plasma proteins, all contribute to a varying extent to the occurrence of oedema.

3. *Albuminuria:* Albuminuria is usually the last sign to appear. It is the result of renal cortical ischaemia. The extent of albuminuria is variable and is considerably influenced by rest and administration of drugs. Albuminuria may suddenly increase independently of the other two signs. Albuminuria in pregnancy may sometimes be due to pyelonephritis, nephrotic syndromes, chronic glomerulonephritis or essential hypertension; all these conditions must be considered in the differential diagnosis.

Additional signs and symptoms

1. *Abnormal weight gain:* The average weight gain in pregnancy is 24 lb. in 40 weeks. Of this, not more than 10 lb. should be gained between the 20th and the 30th weeks of preg-

nancy. A gain of more than two pounds in any one week indicates undue weight gain.

2. *Headache:* Usually occurs in severe pre-eclampsia; severe headache is a sign of impending eclampsia.

3. *Visual disturbances* of the nature of flashes, blind spots, blurring or even total blindness may occur. These signs are a result of papilloedema and retinal vasospasm; partial or total blindness is usually a result of intraocular haemorrhages.

4. *Epigastric pain and vomiting:* These symptoms usually occur in women with impending eclampsia.

5. *Eclamptic fits:* These can usually be forestalled by careful prenatal care. Very rarely, eclamptic fits may set in without any warning signs. In such women, careful assessment reveals that the patient has not been examined medically for some time. Signs of toxaemia sometimes set in rapidly and culminate in eclampsia in a matter of hours. Details of eclampsia and its management are discussed later.

Consequences to the Mother of Specific Hypertensive Disease of Pregnancy

(1) *Immediate:* This varies considerably. Now-a-days, rest, sedatives and induction of delivery before severe hypertension has persisted for too long, have all led to drop in immediate mortality. Theobald (1932) records a 6% mortality following eclampsia and Chesley *et al* (1948) had 10% immediate mortality following eclampsia.

(2) *Remote:* The fall of blood pressure after delivery at one time led to the belief that pre-eclamptic toxaemia was a completely reversible disease with no sequelae. Harris (1924), however, examining patients one year after they had been discharged free of symptoms, found that of 27 who had had eclampsia, 3 had signs of chronic nephritis, and of 55 who had had pre-eclampsia, 33 had signs of renal involvement. Kellogg (1924) drew attention to the condition of recurrent toxaemia of pregnancy. Gibberd (1929) found that after toxaemia, 10% developed chronic nephritis, 40% recovered kidney function completely and 50% were well between pregnancies but developed proteinuria in subsequent pregnancies. Herrick and Tillman (1935) reported on a study of 594 women who had had toxaemia of pregnancy. They found that the death rate was 7 times higher in these women and that 80% of the deaths were cardiovascular.

Browne and Dodds (1939) followed 400 women who had had toxaemia for a period of 6 months to 12 years. 51% of these women had a blood pressure over 130/70. Of those without hypertension, 31 became pregnant again and of these 20 developed recurrent toxaemia. The post-toxaemic blood pressure depended on the severity of toxaemia, duration of toxaemia and the blood pressure on discharge and very slightly on age and parity of the patients. Of the eclamptic patients, 61% showed residual hypertension and 6.5% died. If the limit of hypertension was changed from 130/70 to 140/90 as an index of hypertension, the incidence of residual hypertension dropped to 30.5%.

Treatment

Objectives of treatment include the following

1. To prevent aggravation of the disease and onset of fits.
2. To deliver a child which survives.
3. Delivery to be effected with minimal maternal trauma.
4. To prevent residual after-effects.

Ambulatory Treatment

This is applicable to patients whose systolic pressure does not exceed 135 mm. Hg. and diastolic pressure does not exceed 85 mm. Hg. and in whom oedema and albuminuria are absent or minimal. These patients are advised (i) to take as much rest in bed at home as possible, (ii) to avoid undue exertion, climbing stairs, etc., (iii) to restrict salt during cooking and avoid adding salt at the table, (iv) to come for check-up of weight and blood pressure twice a week, (v) to report occurrence of any new symptoms, and (vi) to take a sedative at bedtime.

If the blood pressure remains under control and oedema and albuminuria do not increase, then ambulatory therapy may be continued. But, on appearance of any of the following signs the patient must be hospitalised:

(i) Elevation of blood pressure to 140/90 mm. Hg. or over.

(ii) Rapid weight gain of more than 3 lb. in a week.

(iii) Appearance of gross oedema.

(iv) Albuminuria 2+ or over.

(v) Appearance of symptoms like visual disturbances, epigastric pain, vomiting and the like.

Hospital Management

Hospital management consists of—

1. General and nursing care

(a) Ensure bed rest; only mild cases are permitted bathroom privileges.

(b) The patient is weighed daily.

(c) The 24-hour urine output chart is maintained and urine tested daily for albumin.

(d) A four-hourly T.P.R. chart is maintained.

(e) The blood pressure and foetal heart rate are checked twice daily.

(f) The patient is given a high protein, low calorie diet with mineral and vitamin supplements.

2. Medical Management

(a) *Control of hypertension:* Bed rest, salt restriction and the use of sedatives like Pulv. Phenobarb., 30 mg. three times daily, go a long way in lowering blood pressure. When simple measures do not succeed, antihypertensive drugs are employed.

(i) Rauwolfia serpentina alkaloids: These have an action on the central nervous system and thus they produce a reduction in peripheral resistance and fall of blood pressure. The dose employed is 0.25 mg.-0.50 mg. twice to three times a day depending on clinical severity of hypertension.

(ii) Hydrallazine has a direct action on the muscular tone of medium-sized blood vessels. It helps in reducing peripheral resistance and, in synergistic combination with reserpine or veratrum alkaloids produces excellent clinical results.

Rakshit (1955) carried out a controlled clinical trial using reserpine

tablets, 0.25 mg. orally 2 to 3 times a day, in 50 cases of pregnancy toxaemia and compared the results with those of 50 control cases treated with rest, diuretics, diet, laxatives, and sedatives like chloral hydrate, potassium bromide, barbiturates, or morphia. He concluded that Rauwolfia serpentina alkaloids cause a gradual, steady and sustained fall of blood pressure. The incidence of eclampsia, abruptio placentae, the persistence of albuminuria, and perinatal loss are all markedly reduced in treated cases.

Menon (1961) was not impressed with the results of a combination of Rauwolfia serpentina alkaloids and hydrallazine derivatives. He found no lowering in the severity of the disease and no improvement in perinatal mortality.

Anjaneyulu and Shastrakar (1959) reported on the use of Tablet Adelphane, which is a preparation composed of reserpine 0.1 mg. and 1.4 dihydrazinophthalazine 10 mg., in dosages of 3 to 6 tablets a day according to clinical severity in a group of 30 toxaemic women. Thirty other toxaemia cases not receiving the drug were studied for comparison. Their results showed that all the nine cases of mild pre-eclampsia were normotensive within 48 hours of treatment. In no case was induction required. All patients progressed satisfactorily to term and no baby was lost. In the control group of 8 mild pre-eclampsia cases, two delivered prematurely and one required induction of labour. Amongst 21 severely toxaemic women, a satisfactory response was obtained in 10 cases as opposed to 4 cases in the 22 control cases. The incidence of complications and perinatal loss was not significantly different in the two groups.

(iii) Guanethidine: This drug has been tried in 12 cases of toxaemia by Dave (1961) in Baroda. Daftary and co-workers (1963) carried out a double blind control trial using 60 mg. of guanethidine in divided doses over a 20-day study at the Nowrosjee Wadia Maternity Hospital, Bombay. Both the groups of workers have noted satisfactory control of blood pressure and postural hypotension was commonly observed in such cases. In the dosages used, other side-effects were not recorded.

Ganglion-blocking drugs have not been found satisfactory. Without exception, their effect on the blood pressure was often slight, unpredictable, brief and unsustained. It is not safe to use these drugs during labour as they are known to cross the placental barrier and cause neonatal ileus.

(b) *Control of oedema:* Bed rest and salt restriction help reduce oedema, but in severe cases diuretics are employed. Chesley and Valenti (1958), and Eastman and Hellman (1961) have reported on the beneficial diuretic effects of both chlorothiazide 500 mg. and acetazolamide (Diamox) 250 mg. in the management of pregnancy oedema.

Hudson (1961) has shown that the diuretic efficacy of chlorothiazide 500 mg. twice daily and hydrochlorothiazide 50 mg. twice daily is comparable. During drug therapy, all patients excrete more sodium and chloride and lose weight. On stopping therapy, sodium and chloride excretion ceases and weight is regained.

Adatia (1961) treated 64 patients of pregnancy toxaemia with tablets of chlorothiazide 500 mg., morning and evening for two weeks or longer. He reported that, except for 5 patients, all others lost weight varying from 4-23 lb.

Use of ion exchange resins: Ion exchange resins were used to induce elimination of sodium from the body. They help convert a low sodium intake into a very low salt intake. Carey and Liley successfully treated four cases with resins. They used 75g. of ammonium resins daily for 3 days followed by 2 days' rest and repetition of the drug again thereafter. These drugs are unpleasant to take and require to be taken in large quantities. Few obstetricians use these drugs in practice.

How long should expectant treatment be continued?

As long as the response to medical measures continues, the expectant treatment is continued until 38 weeks, but if (i) signs and symptoms are severe, (ii) there is a sudden increase in any one sign, or (iii) there is appearance of a new sign, e.g. intense headache, repeated vomiting, epigastric pain, visual disturbances or oliguria, pregnancy should be terminated forthwith.

Methods of termination of pregnancy

1. Low rupture of membranes if presentation is an engaged vertex.

2. If presenting part is high-floating, after rupture of membranes, allow liquor to drain out by digital manipulation.

3. If within 6-8 hours labour pains do not ensue, an oxytocin drip is started and the patient carefully watched.

4. A caesarean section is indicated in the following cases:

(i) In women with coincident obstetric complication which offers a second hazard, e.g. contracted pelvis, malpresentation, etc.

(ii) Obstructive oedema of the vulva: Vaginal delivery may lead to extensive soft tissue injury and sloughing of tissues.

(iii) Severe toxaemia which does not respond to medical measures.

(iv) Impending eclampsia.

(v) Accidental haemorrhage—selected cases.

Eclampsia

Eclampsia is an acute disease peculiar to the gravid and puerperal women, preceded by toxaemia and characterised by convulsions, coma and other symptoms.

Incidence: The incidence is variable in different parts of the country, depending on nutritional standards and the quality of prevailing antenatal care. The leading institutions receive many emergency eclampsia cases; hence, the incidence quoted by such centres is high. This, however, is not a reflection on the standard of obstetric care. All figures must therefore be carefully scrutinised.

Clinical Course

Almost without exception the outbreak of convulsions is preceded for a longer or shorter time by premonitory signs and symptoms indicative of pre-eclampsia. Occasionally, the onset is preceded by a distinct aura, but this is usually lacking. Severe epigastric pain or a feeling of constriction in the chest frequently precedes a fit. Apprehension, excitabi-

Authors	Period of study	Incidence %
Mitra and Das Gupta	1957-1958	1.1
Menon	1923-1929	2.1
	1953-1958	1.6
Upadhyaya and Mishra	1954-1963	0.38-0.78
Choudhury and Chakravarti	1959-1961	1.3
Purandare and Zaveri	1967	
Lewis (Queen Charlotte Hospital, London)	1949-1958	0.12
Eastman and Hellman	1961	0.1-0.2
Mitra, Bhose and De	1958	1.15

lity and hyper-reflexia often precede the onset of a fit.

The eclamptic convulsion may come on at any time. If the patient is awake, she is seen to have a fixed expression of the eyes, the head is turned to one side, the pupils are commonly dilated, and facial twitchings are observed around the mouth. This is the stage of invasion and lasts for only a few seconds. The whole body then becomes rigid, there is tonic contraction of all the muscles, the face is distorted, the eyes protrude, the hands are clenched, the arms flexed, and the legs inverted. This is the 'tonic phase'. It lasts for 15-30 seconds. Suddenly the jaw begins to open and close violently. All the muscles of the body alternately contract and relax in rapid succession. During this stage, the patient may be thrown off the bed and get hurt, or the tongue may be bitten. The face appears congested and there may be foaming at the mouth. This is the "clonic phase". It usually lasts for a minute or so. Gradually the muscles relax, the patient lapses into deep sleep or coma, and long deep stertorous breathing is resumed. Sometimes, eclampsia may occur for the first time after delivery. Puerperal eclampsia usually occurs within the first 48 hours; later than that, it is rare for eclampsia to occur.

Authors	No. of cases	Antepartum fits	Intrapartum fits	Postpartum fits
Menon (1961)	1,151	826 (71.5%)	61 (5.5%)	264 (23.0%)
Bhose and Mitra (1958)	367		305 (83.1%)	62 (16.9%)
Choudhury and Chakravarti (1964)	112		92 (82.2%)	20 (17.9%)
Upadhyaya and Mishra (1964)	338	200 (58.9%)	109 (33%)	30 (8%)

It will be observed that eclamptic fits commonly occur before parturition. In 8%-23% of cases, fits occurred after delivery.

After a fit, proteinuria is the rule. All eclamptic patients have oedema.

Following antepartum eclampsia,

generally the patient goes into labour within a few hours.. Sometimes, labour does not ensue and, under treatment, the patient improves and comes out of coma. The improved state may last for several days and is known as intercurrent eclampsia. It has been known that, in such patients, the eclamptic state may completely subside and pregnancy may continue normally. However, in a majority of cases, eclamptic fits do recur after a variable period of time and in such cases maternal and foetal prognosis is very much worsened.

Bhatt reviewed 15 cases of intercurrent eclampsia who were permitted to continue their pregnancy under strict medical supervision for periods varying from 7 to 38 days. Five babies were salvaged. In no case was a caesarean section required and there was no maternal death. He pleads for a revision in obstetric opinion regarding the management of intercurrent eclampsia and favours a conservative attitude.

Treatment of Eclampsia

Since the introduction of sedatives by Stroganoff (1928) in the management of eclampsia, and its later modification (Stroganoff and Davidovitch, 1937), the main lines of management of eclampsia have revolved around two principles: (i) sedation to lower the patient's sensitivity to perception, and (ii) to prevent afferent impulses from reaching the patient's central nervous system.

The use of bromethol (Dewar and Morris, 1961), intravenous thiopentone (Browne, 1950), veratrum alkaloids (Bryant and Fleming, 1940), chlorpromazine (Menon, 1961) and other drugs in various combinations have been tried by different groups of workers. Literature on this subject is voluminous and cannot be reviewed except in very broad terms. Since the aim of therapy is to control the fits and to improve maternal and foetal salvage rates, maternal and perinatal mortality appears to be the most logical basis for comparison of various therapeutic regimens.

Menon's (1961) regimen: The "lytic-cocktail" — chlorpromazine promethiazine or diethazine-pethidine — is a mixture of drugs introduced in 1950 by Laborit. The mixture is credited with inducing a state of artificial hibernation characterized by hypothermia, hypotension, bradycardia, amnesia, muscular relaxation, reduced metabolism and hypnosis.

Menon (1961) has had an extensive experience with these drugs in the management of eclampsia. He has achieved excellent results. In the years 1955-1958, he treated 402 cases with a maternal mortality of 2.2%. Since he has achieved the best results based on a wide experience, it is imperative to mention the salient features of his method of treatment.

Maternal Mortality and Perinatal Loss

In India, next to anaemia, toxaemia probably accounts for the next major share in the causation of maternal mortality. Masani, Joshi and Daftary (1961) reviewed the causes of maternal mortality at the Nowrosjee Wadia Maternity Hospital over a period of 3 decades. They observed that the overall maternal

Summary of Treatment (Menon, 1961)

1.	Intravenous thiopentone	0.5 g. initially in severe cases.
2.	On admission: 25.0 mg. chlorpromazine + 100.0 mg. pethidine	in 20 ml. of 5% glucose given intravenously slowly
	+ 50.0 mg. diethazine	Intramuscularly
3.	200 mg. pethidine in one litre of 20% glucose	Given slowly intravenously over 24 hours or longer
	+	
4.	50 mg. chlorpromazine or 50 mg. diethazine	Intramuscularly every four hours
5.	Caesarean section	If no clinical improvement in 8-10 hours, and patient is not in labour and cervix not ripe.
6.	Artificial rupture of membranes	In women with no clinical improvement in 8-10 hours, when cervix is ripe, or labour has set in.

mortality had declined from 20/1000 confinements (1931-1935) to about 5/1000 confinements (1956-1960). They attribute the lowering in maternal mortality to improved antenatal care, better drugs — haematinics, antihypertensive drugs, diuretics and antibiotics — improved blood bank services and great improvement in medical personnel. However gratifying may be the above results, it is clear that toxaemia still continues to play a pivotal role in causing maternal deaths. Whereas toxaemia accounted for 2 deaths/1000 confinements at Nowrosjee Wadia Maternity Hospital in the years 1931-1935, it accounted for 0.6 deaths/1000 in the years 1956-1960. Thus, we find that whereas the overall maternal mortality has been reduced to a quarter over 3 decades, the mortality of toxaemia has been reduced to only a third.

Shastrakar and Devi (1961) reviewed 550 maternal deaths from Nagpur over a nine-year period (1952-1960). They found that toxaemia accounted for 7.1% of maternal deaths, and was next to anaemia amongst causes of maternal mortality. Kirloskar (1961) analysed 152 maternal deaths from Hyderabad and she found that toxaemia accounted for 22 deaths in the series.

Toxaemia also contributes to a great extent towards foetal wastage. Peel (1961) stated that one-third of the premature births of known cause were due to pre-eclampsia. Engineer and Mukherjee (1961) reviewed the causes in 130 cases of perinatal deaths in Lucknow and opined that toxaemia was the contributory factor in 8.5% of cases. Naidu (1961) carried out a clinico-laboratory study of the causes of 1795 perinatal deaths. Four hundred autopsy studies were carried out. They estimated that toxaemia accounted for 17.9% of the deaths. Pre-eclampsia was next to birth trauma and thus the second commonest cause of perinatal mortality.

The figures of maternal and perinatal deaths in pre-eclampsia and

eclampsia continue to be high. All efforts must be made in clinics all over India to reduce the hazards of this dread disorder of pregnancy.

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