

ON THE USE OF THYROID EXTRACT IN PUERPERAL ECLAMPSIA AND IN THE PRE-ECLAMPTIC STATE.

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IN a preliminary paper, entitled 'Eclampsia and the Thyroid Gland,'* I brought forward some evidence to show that it was possible to connect the occurrence of some cases of puerperal eclampsia with inadequacy of the maternal thyroid system—thyroid and parathyroid glands. I attempted to show how the principal symptoms of the eclamptic state could be explained in terms of thyroid inadequacy. I shall here shortly indicate some points which seem to suggest that this idea is worthy of consideration.

It is a well-established fact that in normal pregnancy the thyroid gland is enlarged. The significance of this hypertrophy is obvious, because it can be diminished, or prevented altogether, by giving thyroid extract. A larger supply of iodothylin is therefore needed in the pregnant than in the non-pregnant state. In 20 out of 25 cases of pregnancy in which the usual hypertrophy of the thyroid did not occur, albuminuria, and sometimes eclampsia, developed (Lange). In eclamptics the normal enlargement of the gland is said to be absent.

It is generally agreed that the eclamptic symptoms are dependent upon an auto-intoxication, and it seems quite likely that this condition is a result, in the first instance, of inefficient metabolism, and subsequently of imperfect excretion. The whole question of auto-intoxication is intimately associated with the adequate function of the various metabolic organs of the body—the so-called 'defence organs'—and it may be assumed that iodothylin is essential to the efficient working of all the parts of the defensive mechanism. The symptoms noted after complete thyroidectomy, and those observed in some cases of myxoedema and cretinism, clearly indicate a *toxæmia* associated with faulty metabolism and impaired activity of the excretory organs.

It is well known that under the action of iodothylin the meta-

* *Scott. Med. and Surg. Journ.*, June, 1901, and *Trans. Edin. Obstet. Soc.*, vol. xxvi., 1900-1901.

bolic processes of the body are greatly stimulated, and there is a striking increase in the excretion of urea. In eclampsia, and in all conditions of hypothyroidism, the quantity of urea in the urine is much diminished. This is a very important point, for it carries with it the suggestion that the metabolism of nitrogenous substances has not been continued up to the stage of urea formation. Owing to a deficiency of iodothyrim the process has stopped at an intermediate point, and at a stage where the products are highly toxic.

This state of matters is not generally associated with what we recognise as myxœdema, even in its most marked form; the formation of these toxic substances does not seem to follow disease, or even complete excision, of the thyroid body alone.

The symptoms of a typical attack of puerperal eclampsia closely resemble those of complete experimental athyroidea, as produced by the removal of the entire thyroid system in animals. But in eclampsia it is a condition of *temporary athyroidea*; the resulting toxæmia may, according to circumstances, be slight or severe, and the functional activity of the glands may be re-established under appropriate treatment.

It may be said, then, that puerperal eclampsia occurs as a result of some failure in the process of proteid metabolism, and that this failure to deal efficiently with nitrogenous substances is due either to a *deficiency* of iodothyrim or to the *impaired activity* of the secretion. Under these conditions the object of proteid metabolism is not attained, and the final product—urea—is not manufactured.

Much suggestive evidence, both clinical and experimental, could be given in support of the view that the thyroid secretion is an essential factor in the adequate function of those organs which preside over the metabolism of proteid substances. Of these organs the liver is perhaps the most important; so, as a result of thyroid inadequacy, it may properly be regarded as playing an important part in eclampsia.

When a pregnant woman who exhibits eclamptic symptoms is put to bed, and kept on milk diet, the demands made on her thyroid secretion are greatly lessened, and the process of nitrogenous metabolism is again efficiently carried out. Meat diet, besides using up more iodothyrim, yields too little iodine for the manufacture of a fresh supply. In this connection mention may be made of the effects of thyroidectomy in dogs, when some of the animals were fed with meat and others with milk. In the former the mortality was as high as 96 per cent.; in the latter many dogs lived so long as milk diet was continued, but died when a meat dietary was substituted.

These experiments are very suggestive, and on two occasions, where pre-eclamptic symptoms were being satisfactorily controlled by restricted diet, I have seen convulsions occur which seemed to be clearly traced to a meal which included roast pork. In some recorded cases of eclampsia pork is specially mentioned as being the exciting cause of the convulsions, and it is possible that the imperfect metabolic processes following upon the digestion of this substance may give rise to toxins of unusual virulency.

In my former paper I laid special stress on the fact that the arrest of the secretion of urine, by allowing the absorption of the toxins, led up to the convulsions. It is conceivable, however, that cases occur in which the deadly toxins of eclampsia are prepared, and yet, in spite of partial renal inadequacy, no untoward symptoms arise. The organism is supplied with many resources, which enable it to deal with poisons and render them innocuous. But when the renal secretion fails, the other parts of the defensive mechanism will soon be overburdened.

Marked diminution in the quantity of the urinary secretion is probably one of the earliest and most constant of the pre-eclamptic symptoms, and in my former paper I endeavoured to show that it might be dependent upon a deficiency of the thyroid secretion. I indicated some of the ways in which the thyroid gland might, under normal conditions, participate in controlling efficient renal function. It was suggested—(1) that iodothylin exerted some specific action on the kidney; (2) that *urea*—the final product of nitrogenous metabolism when efficiently carried out in the presence of an adequate supply of iodothylin—acted as a powerful diuretic; and (3) that the well-known changes produced by iodothylin on the circulation (vasodilatation) tended to promote and maintain renal activity. It was pointed out, also, that the internal secretion of the suprarenal glands tended to greatly contract the arterioles.

Thus the thyroid and suprarenal secretions, so far as their action upon the arterial calibre is concerned, are antagonistic, and in all conditions of hypothyroidism the arteries are found to be unduly contracted. I suggested that a spasm of the renal vessels, brought about by unopposed suprarenal influence, might be *one* of the factors which led to the arrest of the renal secretion.

From what has been said, it is evident that the real significance of the pre-eclamptic state is that it points to a breakdown of some part of the defensive mechanism. Furthermore, this breakdown is the result of some inadequacy of the thyroid and parathyroid glands, whereby the process of nitrogenous metabolism, instead of

resulting in the formation of urea, ceases with the production of intermediate substances, which when absorbed excite the symptoms of a toxæmia.

In this way the degree of the toxæmia of pregnancy comes to be dependent, directly or indirectly, upon the quantity and activity of the thyroid secretion; the thyroid gland may therefore be given a primary rôle in the causation of eclampsia.

On this view, supported by some suggestive results observed during a prolonged clinical study of the effects of thyroid extract on the circulation, I suggested the use of this remedy in the pre-eclamptic state, and also after the onset of convulsions. In the latter case, however, it was pointed out that a *large* dose of morphia hypodermically was a valuable adjunct to thyroid treatment, because, by inhibiting metabolism, it stopped the formation of poisons, and gave the thyroid gland time to recover itself. It was also noted in these cases that large doses of morphia (gr. $\frac{1}{2}$ to i.) produced profound effects on the circulation; the pre-existing condition of arterial spasm was fully removed. In this way the one essential and all-important indication in treatment—*re-establishment of the urinary secretion*—was fulfilled. Thyroid extract acts powerfully upon the arteries in a similar manner, and under its influence the vessels become even more fully and more permanently relaxed.

In my preliminary communication I was able to record one case of puerperal eclampsia treated by thyroid extract, which occurred in the practice of my friend Dr. Elmslie Henderson, of Kirkcaldy. The results were eminently satisfactory. During the last few months opportunities have been afforded to me of testing more fully the efficacy of thyroid extract in combating the symptoms of eclampsia and the pre-eclamptic state. In view of the great importance of this subject, I propose in the present paper to briefly record some recent experiences without saying much in the way of explanation.

CASE I.—Mrs. S., twenty-five years of age, consulted Dr. Henderson of Kirkcaldy on the evening of Saturday, December 14, 1901, with a view to engaging him to attend her at her first confinement. She was then at the end of the eighth month of pregnancy. She complained of severe headache, continuous of late, but worse in the morning; of sleeplessness; and of nervousness. The daily quantity of urine had for some time been scanty. She was uniformly swollen all over the body; the face was puffy and pasty; the skin was dry; the hands were swollen, and felt leathery from firm tense œdema.

She was advised to go home to bed, and to take nothing but milk. It was arranged to visit her next day, and to have the urine examined; meanwhile a 5-grain thyroid tabloid was ordered to be taken every four hours. Early on Sunday morning (1.45 a.m.) Dr. Henderson was urgently summoned to her, as she had taken a fit. She had wakened

complaining of severe headache, and was given some whisky-and-water. The headache increased in severity, she became comatose, her eyes became fixed, and finally she went into a fit. When seen she was still deeply comatose, eyes staring, breathing stertorously, and highly fevered. She could not be roused. One third of a grain of the sulphate of morphia was injected hypodermically, and up to this point she had had no thyroid extract, as the tabloids had not yet arrived. The patient was watched for some time, and soon fell into a deep sleep. Dr. Henderson then left, but was almost immediately recalled, as another fit had occurred. The patient was in much the same condition as after her first seizure.

After some time she awoke from her stupor, and 10 grains of thyroid extract were given by the mouth. Instructions were left with the nurse to give a 5-grain tabloid every four hours. The urine became solid on boiling.

On Sunday she was carefully watched all day, and an increased quantity of urine was passed. A welcome perspiration was also noted. She was still very drowsy and stupid, and complained much of headache and pain in the epigastrium. Restlessness was also a marked symptom, and she kept tossing about in the bed. She had a slight fit (the last) on Sunday night. The os uteri was undilated.

On the Monday morning marked improvement was evident: questions were answered rationally, and relatives were recognised. The urine was still increasing in quantity, and the skin was no longer dry. The temperature was normal, and the pulse was quite evidently softer. On the Monday night labour pains set in, and on the following afternoon (Tuesday) she was delivered of a dead premature child. In this case the brawny œdema of the arms, legs, and pudenda was very marked, and it rapidly subsided under the thyroid treatment. The urine quickly increased in quantity, and the albumen steadily disappeared. There were no post-partum fits, and the patient made an uneventful recovery. The thyroid extract was continued for a week after the birth of the child.

CASE 2.—With regard to the case of eclampsia, Mrs. L., who was treated with thyroid extract, and reported in my previous paper, I am now able to give some further interesting details.

The patient was attended in this confinement (the third) by Dr. Henderson of Kirkcaldy. She developed eclampsia towards the end of the eighth month of pregnancy; but the labour, which took place at full time, was normal, and resulted in the birth of a living child. Her former pregnancies had been attended by severe and dangerous eclamptic seizures. After her recovery from her third confinement in November, 1900, Dr. Henderson instructed her, in the event of her becoming pregnant a fourth time, to let him know as early as possible. He intended to give her thyroid extract, if it seemed desirable, during the course of pregnancy.

On February 2, 1902, the patient called on Dr. Henderson, and informed him that she was seven months pregnant. When asked why she had not come sooner, she confessed that she had, on her own initiative, been taking thyroid tabloids regularly since the third month of pregnancy. So greatly was she impressed by the beneficial results of this treatment during her previous pregnancy, that she desired to test the effects of the remedy again.

She stated that she felt altogether different in this pregnancy. She had no sickness; no swelling of the face, arms, or body; no giddiness; no blindness, no headaches even. She said that she had never felt better in her life.

On examination it was noted that there was no œdema, no diminution in the quantity of urine, and no albuminuria. Usually a large stout person, and especially so during her pregnancies from superadded solid œdema, she was on this occasion precisely the reverse. Her altered

appearance—suggestive of overdosing with thyroïdin—so impressed Dr. Henderson that he discontinued the thyroid treatment at this time.

A month later the patient was not so well. She had caught a chill, and complained of headache and a general feeling of malaise. The unusual emaciated appearance, already noted before the thyroid treatment was stopped, was now disguised by a slight degree of general œdema, and upon inquiry it was found that the daily quantity of urine was much diminished. The cold nitric acid test showed the presence of a considerable amount of albumen.

The patient was put to bed, ordered a restricted diet, and thyroid treatment (10 grains daily) was immediately recommenced. In a few days the threatening symptoms were under control, and shortly afterwards (March 7) I saw her. She was again abnormally thin about the face, and there was no œdema of the hands or feet; she felt well, and wished to resume her household duties. The pulse was rapid—115 per minute—and of fair pressure; the skin was warm, and the urine, which was being secreted in satisfactory amount, showed no traces of albumen, even to the nitric acid test. There had been no cessation of the fetal movements, though they had not been so strong of late; the fetal head was found to lie well down in the pelvis, but the heart sounds could not be heard. The dose of thyroid extract was reduced to 5 grains daily.

The patient was allowed to get up, and everything went on well till March 13, when, after a short normal labour, she was delivered of a dead premature infant. There were no abnormal symptoms either at the time of labour or during the puerperium. The child had probably been dead for seven or ten days.

CASE 3.—Mrs. D., aged twenty-three, consulted Dr. Hope Fowler on January 4, 1902, on account of severe headache and dimness of vision. She had just entered upon the seventh month of her first pregnancy. Her face, hands, and body were greatly swollen with the same kind of firm solid œdema previously described as characteristic of some cases of eclampsia; her condition resembled that of a patient in an advanced stage of myxœdema.

The pulse-rate was found to be 50 per minute; the artery was greatly contracted, and it was with difficulty that the finger could obliterate the pulse wave. I have already directed attention to the possible significance of an *abnormally slow pulse* towards the end of pregnancy, especially if it persists, and this was the feature that made Dr. Fowler suspect albuminuria.*

In this patient all the typical symptoms of the pre-eclamptic state, including great diminution in the quantity of urine, were present to a very marked degree, and the urine boiled nearly solid with albumen. She was kept in bed, and was given nothing but milk for ten days. On January 15 Dr. Fowler kindly asked me to see her with a view to treating the condition with thyroid extract.

I found her very much swollen all over the body; the face was puffy and bloated, and the forearms were so hard and brawny that it was difficult to pick up a fold of skin. The urine had only increased very slightly under the milk diet, and albumen was still present to the extent of 2 grains to the ounce. The pulse was now 55 per minute; the artery was contracted, and the characters of the sphygmogram indicated a very high blood-pressure.

A 5-grain tabloid of thyroid extract was ordered to be taken three times a day, and after 30 grains had been taken the arteriometer showed that the calibre of the radial artery was already enlarging. The pulse-rate was considerably accelerated, but the quantity of urine was not yet noticeably increased. The œdema, however, was beginning to get softer.

* 'Encyclopædia Medica,' art. 'Pulse,' p. 187.

On January 21 the tabloids were given every three hours, and a marked effect on the amount of urine secreted was noted. The increased doses of thyroïdin caused much flushing of the skin and profuse perspiration, but the effects on the kidneys and on the œdema were not immediate. In two or three days, however, the quantity of urine was *enormously* increased, and the patient described herself as 'melting away.' On January 29 the face and arms were quite thin, and the œdema of the body had nearly disappeared. The patient remarked that she was now thinner than in her normal condition of health.

The thyroid extract was given steadily for seventeen days, then stopped for a fortnight, and recommenced with a dose of 5 grains daily. During the treatment, fish, bread, and light puddings were allowed in addition to milk, and yet the albumen steadily decreased till it was entirely absent.

On February 2 the patient was allowed to get up, and returned to ordinary diet. She was soon able to resume her household duties, and the œdema showed no signs of returning. The pulse-rate—quickened since the commencement of the thyroid treatment—remained at between 85 and 95 per minute, and there were signs of arterial dilatation and lowered blood-pressure. The daily quantity of urine remained satisfactory, and it remained free of albumen.

The patient kept at work till the morning of March 10, when, after a normal labour, a dead premature infant was born. The puerperium was uneventful.

My friend Dr. Ballantyne, who kindly examined the fœtus, was of opinion that death had occurred from three to five weeks before expulsion.

CASE 4.—Mrs. P., aged thirty-nine, 2-para, was seen on February 27, 1902. She complained of severe headache, giddiness, and attacks of vomiting. For several weeks she had noticed that the daily secretion of urine was less than usual, and also that her legs were getting swollen. There was no definite œdema of the face or hands. The urine was examined, and on boiling threw out a thick precipitate of albumen.

Next day a 5-grain thyroid tabloid was given every four hours during the day, and she was advised to remain as much as possible in bed. Milk, fish, bread, and light articles of diet were allowed.

On March 3, after 50 grains of thyroid extract had been taken, there were obvious symptoms of 'thyroidism.' The pulse rate was accelerated, the radial calibre was enlarged, there was marked flushing of the skin, perspiration, and slightly increased secretion of urine. The albuminuria was also somewhat less, the headache had disappeared, and there had been no vomiting for two days.

On March 5 there was a striking increase in the quantity of urine, and now no albumen was found on boiling it. The cold nitric acid test, however, showed a faint white ring at the junction of the urine and acid.

On March 7 urine was still being passed in satisfactory amount, and the patient noticed that she had now become considerably thinner about the body and lower limbs. The nitric acid test still showed a mere trace of albumen.

On March 11 the patient felt well again, and was allowed to remain up for a longer period during the day. The increased quantity of urine was maintained, and albumen was now practically absent. She was still taking 10 grains of thyroid extract daily. Fœtal movements were felt by palpation, and the fœtal heart was heard.

On March 15, as some symptoms of 'thyroidism' were still apparent, the tabloids were discontinued. Two days later, however, headache and vomiting returned, and the quantity of urine was again diminished. There was also a return of albuminuria, which was now readily detected

on boiling the urine. Thyroid treatment—10 grains daily—was recommenced.

On the following day she felt much better, and on March 19 I safely delivered her of two fine infants—a girl and a boy. It was necessary to use the forceps for both children, owing to a slight contraction at the brim, but otherwise everything was quite normal.

The mother made an uninterrupted recovery, and on March 21 the urine was free of albumen. Thyroid extract was not given in this case during the puerperium. Both children are at present strong and healthy.

I have now shortly related the results obtained from the use of thyroid extract in one of the most serious and dreaded complications of pregnancy. In Case 1 the fact that the child was born dead may have had something to do with the satisfactory termination, but the absence of post-partum fits in this instance, and also in the other cases, is noteworthy. In cases of puerperal eclampsia treated by other means, statistics prove that post-partum fits occur in 50 per cent. of them. Under these circumstances recovery is slow, and symptoms may persist for days. The remarkably rapid disappearance of all the unfavourable signs under thyroid treatment is in striking contrast to this, and must be seen to be fully appreciated.

In Case 3 the fœtus was evidently alive after the patient was absolutely free from all her pre-eclamptic symptoms, but pregnancies in which anuria and albuminuria develop are specially liable to result in premature labours with dead infants. McKerron,* in a recent valuable paper on 'Suppression of Urine after Labour,' has drawn attention to this fact, and also makes the interesting observation that in such cases *vomiting* is the most uniform and striking symptom. Vomiting is also one of the most important signs of the pre-eclamptic state, and it invariably improves when diuresis is re-established under the action of thyroid extract. In the post-partum eclamptic state, as described by McKerron, where suppression of urine is the most prominent among a set of symptoms, it seems likely that thyroid extract may also prove itself to be a remedy of great value, if only from its remarkable power of re-establishing the urinary secretion when sufficiently pushed to produce its full effects on the circulation.

In Case 4 *vomiting* was a marked feature, and the progress of this case under thyroid treatment was specially gratifying.

The results obtained in all the cases, however, were too definite and too striking to be ascribed to mere coincidence. Anyone who has used thyroid extract in a large variety of cases, and who has confined his observations to the effects of the drug upon the circula-

* *Journ. of Obstet. and Gynæcology*, vol. i., April, 1902.

tion alone, cannot fail to be impressed by the widespread therapeutic possibilities of the remedy. But the preparation used must be fresh and absolutely reliable. This is a difficult matter, because the amount of iodothyron in different glands varies considerably; therefore one 5-grain tabloid may contain much more of the active substance than another. When the tabloids are exposed to the air and light, or if they are kept too long in stock, their activity may become greatly impaired. I feel sure that these facts help to explain the disappointing and contradictory results of thyroid treatment in the hands of different observers.

Thyroid extract is not a dangerous remedy, unless in exceptional cases; but it is necessary, as in the use of any powerful drug, to carefully watch the results. Patients react very differently, and those suffering from goitre or myxœdema, or any other condition of hypothyroidism, are peculiarly sensitive to its effects. It is suggestive that in eclamptic patients symptoms of 'thyroidism' seem to be very readily induced.

Many of the symptoms which patients develop under thyroid treatment are probably due to the profound circulatory changes produced by the drug. The earliest and constant effect is a marked acceleration of the pulse-rate, and this is followed in a few days by increased warmth and flushing of the skin, due, no doubt, to the uniform enlargement of the calibre of the arteries. This is succeeded by perspiration, and still later by obvious diminution in the body-weight. This loss of flesh, or it may be removal of fluid from the body, is invariably noted, and there is ultimately much increased diuresis. But in the eclampsia cases increased secretion of urine was *not an early effect* of this treatment; it was some days before adequate function of the kidneys became restored.

In the use of this remedy in eclampsia and in the pre-eclamptic state, can the strikingly beneficial results obtained be brought about entirely by the changes produced on the circulation? Supposing we admit—what may be taken as an established fact—that the drug possesses a specific action in enlarging the calibre of the vessels, that it fully relieves a condition of arterial spasm, is this a sufficient explanation of the disappearance of symptoms of a very threatening character? Under its use the renal vessels will become relaxed, and then re-establishment of diuresis will occur, for reasons which Sir Lauder Brunton's researches on the action of certain diuretic drugs have clearly shown. Then the beginning of the successful termination of the case is accomplished.

I am satisfied that the value of *morphia* in eclampsia is to be

explained in the same way. In cases of ordinary puerperal eclampsia a hypodermic injection of morphia—and preferably a large dose—has no detrimental influence on the secretion of urine, but is actually the agent which promotes the re-establishment of diuresis. A large injection always produces effects on the circulation precisely similar to those of ‘thyroidism,’ and profuse sweating occurs. Increased secretion of urine is not an early effect, for the period at which the renal vessels become relaxed—as under thyroid treatment—is variable.

The nervous phenomena of eclampsia are also controlled by morphia, but this is of secondary importance. The fact that the remedy *re-establishes* diuresis in eclampsia instead of abolishing it, is one not yet properly appreciated.

The fear, too, of the dangerous cumulative effects of morphia, when renal action is in abeyance, seems to be greatly exaggerated, and unwarranted by facts. In the case of strychnine some recently-made experiments show that such a theory is incorrect.*

With regard to the undoubted beneficial effects of large *saline infusions* in eclampsia, I have elsewhere pointed out that this is primarily brought about by an enlargement of the arterial calibre—relaxation of spasm.† After such an infusion, the patient is in a condition which compares well with that of ‘thyroidism,’ and re-establishment of the renal secretion results. Here also the effects are not immediate; they may not occur for twenty-four or thirty-six hours. But the rationale of its action is the same as in the morphia or thyroid treatment, and probably in other methods of successful treatment the same principle is involved—relaxation of the blood-vessels resulting in diuresis. Saline infusions may act, in the first instance, by diluting the toxic blood, as has been suggested, but the later diuretic action is a much more important one.

While it is possible that the excellent results of thyroid treatment in eclampsia are mainly due to the re-establishment of diuresis following upon the circulatory phenomena produced by the drug, yet I am disposed to think that there is something more subtle in its action. In eclampsia the remedy would appear to be something of the nature of a specific, and possibly by favouring metabolism in some unknown way it is able to counteract the effects of the intoxication. It may also assist in the removal of certain urinary products which have accumulated in the tissues previous to the onset of con-

* Meltzer and Salant, The Effects of Subminimum Doses of Strychnine in Nephrectomized Rabbits' (*Journ. of Experimental Medicine*, vol. vi., No. 2).

† 'Encyclopædia Medica,' p. 194.

vulsions. These will be excreted *early* in the urine when diuresis is again established.

Many suggestive facts tend to support the view that eclampsia is connected in some way with thyroid or parathyroid inadequacy, but as yet our knowledge of the functions of these glands—especially the parathyroids—is very incomplete. There is some evidence to show that the parathyroids normally deal with entero-toxins, and render them innocuous.

Meanwhile, I believe that I have established the interesting and important fact, namely, that *by producing symptoms of 'thyroidism' in an eclamptic patient the re-establishment of the renal secretion is secured*, and albuminuria steadily disappears.

Before the functions of the kidneys are fully restored the other unfavourable features—vomiting, headache, blindness, etc.—ameliorate, and the prognosis to the mother, when treatment is not delayed too long, is exceedingly favourable.

As a summary of the views here expressed regarding the treatment of eclampsia, the following points may be stated :

1. Deficiency or impaired activity of the thyroid secretion leads to a derangement of some part of the 'defensive mechanism.' Toxic substances (intermediate or imperfectly converted products of nitrogenous metabolism) then *gain entrance* into the blood, and this coincides with the onset of the pre-eclamptic state.

2. Diminution, and ultimately arrest of the secretion of urine, occurs, which allows *absorption* of the toxins, and this culminates in the convulsions.

3. The *re-establishment of the renal secretion* is the one essential and all-important indication in the treatment of eclampsia.

4. By producing symptoms of 'thyroidism' in an eclamptic patient the re-establishment of diuresis is secured.

5. When symptoms of 'thyroidism' are produced, it signifies that the bloodvessels are fully relaxed and that arterial spasm is removed.

6. A *large* hypodermic injection of morphia or a large saline infusion produces effects on the circulatory system quite similar to those of 'thyroidism.' Both these methods of treatment lead to a general dilatation of the arteries, and result in the re-establishment of renal function. The rationale of the action of other successful methods of treatment is probably similar.

7. Diuresis does not occur as an immediate effect of the general enlargement of the arterial calibre, produced by thyroid extract, morphia, or saline infusions, because the period at which relaxation of the renal vessels occurs is variable.

8. Morphia counteracts the nervous phenomena of eclampsia, and temporarily inhibits metabolism ; but the fact that a large hypodermic injection *re-establishes* diuresis, instead of abolishing it, is one of prime importance, and is not fully appreciated.

9. The fear of the dangerous cumulative effects of morphia, when renal action is in abeyance, is much exaggerated, and is unwarranted by facts. Recent experimental evidence tends to prove that such fears are groundless in the case of strychnine.

10. Under thyroid treatment many of the unfavourable symptoms ameliorate *before* the functions of the kidneys are fully restored, and post-partum fits apparently do not occur. If this treatment be commenced early, the prognosis as regards the mother should be very favourable.

11. Thyroid extract—apart from producing beneficial effects from its action on the circulation—may counteract the auto-intoxication by favouring metabolism in some unknown way. It may possibly have some specific action in eclampsia from its power of rectifying a derangement of the 'defensive mechanism,' or from its ability to render certain toxic substances innocuous.

12. In view of a probable relationship between the thyroid gland system and the conditions which lead to the formation and absorption of toxins in pregnancy—culminating in eclampsia—treatment by thyroid extract should be preferred to that of morphia or saline infusions. Thyroid extract would seem to act more powerfully and permanently on the circulation than these other methods, but a combination of morphia and thyroid extract is sometimes invaluable.