gathering impulse of despair, he disappeared and left no sign.

This little story must strike with a chill upon anyone impatient for the advance of knowledge, and especially upon such as are inclined to assume the use of the scientific method to be synonymous with the possession of the scientific mind. Experience fully proves that this assumption is unsound, for there is no limit to the narrowness of the field within which the scientific method may be limited while the rest of the mind is uninfluenced. Even if that assumption is not maintained there are several grounds on which has been defended the proposition that a man of science does well not to traffic very freely with new ideas. It is thought that the necessary concentration on a limited problem is apt to be attenuated by the use of any general intellectual activity. A proposition more worthy of serious attention is that which declares that scepticism and suspended judgement are the very essence of the scientific mind and scarcely to be depended on too much. The conception is no doubt true when its elements are exactly defined. Without such definition these venerable phrases may very easily become mere snares; this is because they are apt to be the expression not of the principles they profess to represent but of far more deeply ingrained and potent impulses.

The mind delights in a static environment, and if there is any change to be itself the source of it. Change from without, interfering as it must with the sovereignty of the individual, seems in its very essence to be repulsive and an object of fear. A little self-examination tells us pretty easily how deeply rooted in the mind is the fear of the new, and how simple it is when fear is afoot to block the path of the new idea by unbelief and call it scepticism, and by misunderstanding and call it suspended judgement. The only way to the serene sanity which is the scientific mind—but how difficult consistently to follow—is to give to every fresh idea its one intense moment of cool but imaginative attention before venturing to mark it for rejection or suspense, as alas nine times out of ten we must do. In this traffic it is above all necessary not to be heavy-handed with ideas. It is the function of notions in science to be useful, to be interesting, to be verifiable and to acquire value from *any one* of these qualities. Scientific notions have little to gain as science from being forced into relation with that formidable abstraction "general truth." Any such relation is only too apt to discourage the getting rid of the superseded and the absorption of the new which make up the very metabolism of the mind.

VII

In making this small survey of the simpler reflections that are suggested by commemorative occasions such as this, three general conceptions have presented themselves rather prominently. Some of them at least have a practical bearing and we should therefore be very unworthy disciples of the Master we celebrate if we did not give them what point we can by a particular reference.

The first of these ideas is the familiar truth that if any human institution is looked into at all closely it is found, however admirable its ostensible purpose, to be built out of a strange mixture of elements and to comprise motives many of them odd and some of them ugly. Memorial ceremonies show themselves to be of this class, and thereby demonstrate that they possess a thoroughly natural origin. In these mild disclosures there is nothing to dismay, and no one need be disconcerted by the homely skeletons in the cupboards of folk-lore. At the same time they perhaps have a use in explaining why the stimulation and enlargement of mind afforded by such commemorations are sometimes less potent than we could wish.

The second conception that emerges is the suggestion that with the process of time it will become increasingly difficult to separate the commemoration of the dead from the responsibility for their treatment during life, or to believe that posthumous honour is in any real sense a reparation for the dead, or a discharge of the liability of the living. It will become less and less possible to regard the discoverer of truth as responsible for the propagation of it, and charged with the duty of converting a stiff-necked generation.

The third and last idea on which our discussion has converged is that if mankind is to profit freely from the small and sporadic crop of the heroically gifted it produces, it will have to cultivate the delicate art of handling ideas. Psychology is now able to tell us with reasonable assurance that the most influential obstacle to freedom of thought and to new ideas is fear; and fear which can with inimitable art disguise itself as caution, or sanity, or reasoned scepticism, or on occasion even as courage.

We may now attempt for a final moment to link these speculations with our primary theme. In his mental environment Hunter must be regarded as a happy man. He lived in the relative intellectual freedom of the best part of the eighteenth century, before its bland sunshine had died in the smoke of industrialism, and before the French Revolution and the reaction to it had deadened speculative thought. He saw, as from a peak in Darien, the illimitable ocean of biology before him and he addressed himself unhesitatingly to explore it all. It was in the general level of knowledge and in instrumental equipment that he was less fortunate. When a new Hunter appears he will not be held back by an undeveloped science and he will find this College able to give him all the facilities with which it has been munificently endowed. Let us hope that he will also find an intellectual environment where even his most revolutionary ideas will be planted in a nourishing soil and bathed in a genial air.

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HIGH BLOOD PRESSURE AS AN EARLY SIGN OF TOXAEMIA OF PREGNANCY*

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The purpose of this paper is to call attention to the fact that an elevation of blood pressure in toxæmia of later pregnancy may precede the appearance of albumin in the urine.

Mahomed (1874) appears to have been the first to demonstrate that "increase of tension on the arterial system" might precede the albuminuric stage in the glomerulo-nephritis following scarlet fever. At that time, however, there was no very accurate method of measuring blood pressure, and Riegel (1884) stated that the albuminuria and the rise of blood pressure were almost synchronous. In 1925 Koch, supporting Volhard's theory of a generalized arteriolar spasm as a cause of ischaemia and consequent injury to the kidney, stated that during convalescence from scarlet fever there occurs, in the majority of cases, a rise in blood pressure, as a "consequent or concomitant phenomenon of the immunization processes going on in the body." This, he said, might after a day or two fall to normal without further demon-

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strable consequences, but it might also be followed by albuminuria and haematuria, and by an acute diffuse glomerulo-nephritis. His estimations were made by the Riva-Rocci sphygmomanometer, the systolic pressure being measured by palpation and the diastolic by auscultation. In Koch's cases the albuminuria appeared a day or so after the rise in blood pressure, which was in the cases he reported very slight (highest 132 mm. systolic), and a complicating factor might well have been the elevation of temperature that not infrequently occurs at this stage of the disease. In pregnancy, of course, such a complicating factor does not appear. Last of all came the observations of Steiner (1928), who disagrees with Koch's conclusions, and states that in his experience the glomerulo-nephritis following scarlet fever is certainly primary, and the rise in blood pressure only begins when the urine is already abnormal.

There appear to be but few references in literature to the fact that the albuminuria of pregnancy may be preceded by a rise in blood pressure, though Fishberg states that sometimes hypertension may precede the albuminuria, and Theobald (1929) has recorded two cases of eclampsia in which albuminuria was absent, though the blood pressure was raised. On the other hand, Izod Bennett (1929) says: "I have the impression, and I think it is a general impression, that the hyperpiesia (in the renal complications of pregnancy) does not occur until albuminuria or some other evidence of renal involvement is present." The question is of great theoretical importance, both from the point of view of the causation of the kidney lesions in glomerulo-nephritis and eclampsia, and of the etiology of hyperpiesia. It is, however, chiefly with the clinical significance of the observation that I am concerned in the present paper.

CLINICAL INVESTIGATION

In the ante-natal clinics at University College Hospital, blood pressure measurements are made by means of a mercurial manometer (Baumanometer), the auscultatory method being used for both systolic and diastolic estimations. Blood pressure is estimated and the urine examined once a month till the thirtieth week, fortnightly till the thirty-sixth week, and thereafter at weekly intervals till delivery. If albumin is found in the ordinary way a catheter specimen is obtained, and only the result of that is entered in the record. The reagent used is a cold saturated solution of salicyl-sulphonic acid. In this way very accurate records are obtained, and one is sometimes enabled to detect abnormalities in their earliest stage.

Altogether the records of upwards of a hundred cases of toxæmias of late pregnancy have been examined, but for various reasons—because they were examples of actual or possible chronic nephritis, or of albuminuria without a rise of blood pressure at any time (the toxæmic nature of the condition being therefore doubtful)—the majority had to be rejected. There were left forty-eight cases bearing on the present discussion. Out of this total the albuminuria and the hyperpiesia were discovered at the same time in thirty-five. This does not necessarily mean that they began at the same time, but possibly the examinations were not frequent enough to detect the disorder in its earliest stage. In the remaining thirteen hyperpiesia preceded the albuminuria by periods ranging from eleven to eighty-nine days. The following are three typical examples.

Case 1 (550/31).—M. C., aged 24; first pregnancy; previous history good. First seen December 11th; expected date of delivery July 20th; B.P. 120/84, albumin *nil*. May 14th: B.P. 135/75, albumin *nil*. May 28th: B.P. 140/100, albumin *nil*; no symptoms. June 4th: B.P. 142/84, albumin *nil*; no symptoms, no oedema. June 15th: B.P. 154/92, albumin +, and slight trace of oedema. Admitted June 18th. June 20th: Trace of albumin. June 26th: Albumin 1 per 1,000.

July 2nd: Albumin 1.5 per 1,000. With rest in bed the blood pressure fell gradually, and was 110/65 just before labour began, after induction by bougies, on July 3rd. In this case sixty-two days elapsed between the rise of blood pressure and the appearance of albuminuria. During all this time there were no symptoms to draw attention to the fact that the patient was in any way abnormal.

Case 2 (554/31).—I. R., aged 30; first pregnancy; previous health good. First seen February 12th: B.P. 150/90, albumin *nil*; advice given. March 12th: B.P. 130/85, albumin *nil*; April 9th: B.P. 128/88, albumin *nil*. April 23rd: B.P. 140/90, albumin *nil*. May 7th: the same. May 14th: B.P. 145/90, albumin *nil*. May 28th: B.P. 140/95, albumin *nil*; June 11th: B.P. 145/100, albumin *nil*. June 25th: B.P. 170/100, albumin trace. Admitted June 29th. During all this time there had been no symptoms except headache on April 23rd, which disappeared, but returned in a very severe form on June 22nd. After admission the blood pressure fell with rest and eliminative treatment to an almost normal level, and never again exceeded 135/86. Albumin persisted until delivery on July 7th, but was never more than a very small trace. Seen on September 2nd following; albumin was absent and B.P. 138/80. There were no apparent cardio-vascular changes. The high blood pressure at the first visit on February 12th was noteworthy. Its possible significance will be referred to later.

Case 3 (246/31).—E. Z., aged 24; one pregnancy, a year previously, complicated by albuminuria, but healthy child born at term. First seen January 4th: B.P. 124/80, albumin *nil*. February 11th: B.P. 120/80, albumin *nil*. March 4th: B.P. 144/80, albumin *nil*. March 18th: B.P. 152/80, albumin +. Admission to hospital refused. April 1st: B.P. 158/110; albumin +. Delivered April 2nd. Seen October 1st: No albumin, B.P. 126/76. In this case the blood pressure was raised for fourteen days prior to the appearance of albumin, and during this time, as in the other two cases, the patient seemed perfectly normal.

The following tabular statement gives the essential details in thirteen cases.

Record Number	Age	No. of Previous Pregnancies	Number of Days Albumin preceded by Rise of Blood Pressure	Other Abnormal Findings Accompanying Raised Blood Pressure before Albumin Appeared	Previous History	Remarks
179/31	38	3	48	None	Albumin 1st pregnancy	—
550/31	24	0	62	None	Good	Slight trace of oedema at same time albuminuria appeared.
246/31	24	1	14	None	Albumin 1st pregnancy	Twin pregnancy.
547/31	22	0	60	None	Good	Rise of blood pressure to 138/92 (normal 125/85) first occurred at 30 weeks; it then became normal for about 4 weeks, but afterwards rose again with albuminuria.
902/31	35	8	14	None	Good	Trace albumin first found when blood pressure was 160/94, but increased rapidly to 4 per 1,000.
880/31	40	1	30	None	Good	Concealed accidental haemorrhage, Caesarean section—live child.
989/29	21	0	22	Pruritus only	Good	—
638/30	33	1	53	None	Good	Twins.
994/30	24	0	89	Headaches 5 days before albumin	Good	—
989/30	21	0	35	None	Good	Blood pressure at first visit (Sept. 8) was 146/108, albumin 0; Sept. 25, blood pressure 105/84, albumin 0; Oct. 6, blood pressure 144/104, albumin 0; Oct. 13, albumin +.
129/29	19	0	11	None	Good	Had slight non-febrile pyelitis.
1073/31	20	0	42	Oedema of feet	Good	Instability of blood pressure notable.
554/31	30	0	64	Headache and slight swelling of ankles. Nausea occasionally	Good	Instability of blood pressure notable.

Though the table is self-explanatory, it is necessary to emphasize that while the period elapsing between the rise of blood pressure and the onset of albuminuria varied between eleven and eighty-nine days, in only four of the cases was there during that time any symptom to draw attention to the fact that the patient was abnormal. The importance of routine estimation of blood pressure is evident; for there can be no doubt that it provides, in many cases at least, an earlier indication of the presence of toxæmia than does examination of the urine. It is noteworthy, too, that sometimes the blood pressure rises slightly at a comparatively early stage of pregnancy, any other demonstrable abnormality being absent, only to subside and remain at a normal level for some weeks. When this occurs it will usually be found that a more permanent rise takes place later, followed in due course by albuminuria. This was so in cases 547/31, 989/30, 1073/31, and 554/31 (see last column of table). It seems as if there is in these cases a curious instability of the blood pressure, and in this connexion one calls to mind the statement of Elwyn that there is an increased irritability of the vegetative nervous system in pregnancy, and that this leads to a greater tendency to vaso-constriction. At any rate, there seems good reason to believe that a temporary slight rise in blood pressure in the earlier stages of pregnancy may be taken as a warning of possible trouble later.

SUMMARY

1. It is shown that in the toxæmia of later pregnancy a rise of blood pressure often precedes by a prolonged period the onset of albuminuria.

2. During the interval between the rise in blood pressure and the appearance of albuminuria (varying in the

reported cases from eleven to eighty-nine days), there are usually no symptoms or signs to suggest that the patient is in any way abnormal.

3. There is some evidence that there may be, in the earlier stages of the pregnancy of patients who later develop toxæmia, a temporary elevation of the blood pressure, which soon subsides, and which may be an expression of increased neuro-muscular irritability and of a greater tendency to vaso-constriction in such patients.

4. The importance, for the timely diagnosis of toxæmias of pregnancy, of routine estimations of blood pressure is emphasized. When these are made, treatment can be commenced at a very early period, with the obvious advantage of minimizing the risk of eclampsia and of chronic nephritis.

5. The term "albuminuria of pregnancy" is a bad one, and is no doubt responsible for much of the permanent kidney damage that has in the past been a sequel of the toxæmia of late pregnancy. Its use has pushed unduly into the foreground the albuminuria, which is really a late symptom, and has therefore tended to obscure the early hyperpiesis, and has thus been the cause of dangerous delay in diagnosis and treatment.

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SYNTHALIN IN THE TREATMENT OF DIABETES

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In November, 1926, a paper was published from the late Professor Minkowski's clinic in the University of Breslau by Frank, Nothmann, and Wagner¹ entitled "Synthetically prepared substances with an action similar to that of insulin on normal and diabetic subjects," in which the authors stated that their work had been undertaken in the erroneous belief that tetany following parathyroidectomy was associated with hypoglycaemia, and with the knowledge that other work had suggested that tetany in children was connected with guanidine poisoning.

Deciding for these reasons to investigate the effect on the blood sugar of animals of injections of guanidine, Frank and his colleagues found that they produced very severe hypoglycaemia and convulsions indistinguishable in character from those which are known to follow heavy doses of insulin, but with the remarkable difference that animals convulsed by guanidine could not be rescued by intravenous injections of glucose. The next step was the endeavour to modify the chemical structure of guanidine in such a way as to eliminate its toxicity and retain its hypoglycaemic power. The original paper claimed that this had been successfully done, and that the new guanidine derivatives, which were called synthalins, not only

had an action indistinguishable from insulin, but also retained their potency when administered by the mouth.

The experimental evidence described in support of this contention was very strong, and may be briefly summarized as follows:

1. Animals convulsed by the synthalin administered by injection could be rescued by glucose intravenously.

2. After total extirpation of the pancreas from dogs the resulting high blood sugar could be reduced by synthalin, and in dogs rendered diabetic by partial extirpation both hyperglycaemia and glycosuria could be controlled.

3. After intra-arterial injection of synthalin a dog had less sugar in the blood of the femoral vein than in that of the artery.

4. Controlled cases of human diabetes were recorded, in which on fixed diets the glycosuria diminished by 40 to 50 grams daily when synthalin was taken by the mouth.

5. Acid bodies in the urine of diabetics diminished after the use of synthalin, and this suggested that more sugar was used as the result of the administration of the drug.

No detailed account of their clinical results was given at the time, but it was stated that the general results in seventy cases were good, and, in addition, the claim was made that two cases previously refractory to insulin had been successfully treated, one of which was complicated by pulmonary tuberculosis.

Towards the end of 1926 the action of synthalin was discussed by the Association of German Physicians,² and there was fairly general agreement on the following points:

1. It was not advisable to use synthalin in severe acute cases or in children.

2. The most suitable type of case was the milder diabetic with a total of about 30 to 40 grams of sugar in the daily urine on a fair diet.

3. Previous long insulin treatment, while not a final contraindication, seemed, in some way unknown, to make a patient refractory to synthalin. Transfer from insulin had to be slowly and carefully carried out.