in about 5 minutes, is maximal in 15 to 20 minutes and is complete in about 4 hours. This dye may be used as a time test, or as a quantitative test for each kidney separately.

Intestinal obstruction.—In intestinal obstruction and pyloric stenosis blood urea is often raised and may be as high as in uræmia. The kidneys are probably not implicated to any great extent and the cause is not clearly understood. These patients are poor operative risks, but the intensive administration of fluid and sodium chloride in the form of normal saline relieves dehydration, decreases the blood urea, diminishes alkalosis and increases blood chloride, thus rendering the patient more fit for surgical treatment.

In *obstetric practice* blood urea estimations are used in the differential diagnosis of albuminuria. If this condition is the result of pregnancy toxæmia the blood urea usually shews little change and high values, above 50 m.gms. per cent., suggest that the albuminuria is due to an exacerbation of a pre-existing nephritis and hence the prognosis is less satisfactory.

Conclusion.

It has been seen that a clinical investigation and an ordinary urine examination must always precede special urine tests for renal function.

Of these special tests the blood urea and urea concentration tests are most important, but both will be negative unless renal damage is extensive and both are misleading in nephrosis; it is probable that they should be superseded by Van Slyke's Clearance test. Estimation of cholesterol is useful in albuminuria of doubtful nature, while excretion of dyestuffs is employed in surgical conditions. The other tests mentioned, though of great intrinsic interest, are not essential to the clinician in the diagnosis and treatment of renal disease.

INTRACRANIAL ANEURISM.*

By C. ALLAN BIRCH, M.D., M.R.C.P., D.P.H.,

Physician, North Middlesex County Hospital.

Intra-cranial aneurisms are not at all rare although it is only in recent years that much attention has been paid to them. Most practitioners have met with an occasional case so that it is not surprising that in this hospital with a large number of acute cases we should have had four examples in the last few months. The frequency of intra-cranial aneurism is indicated by the fact that Fearnside¹ found that at the London Hospital between 1907 and 1913 there were 44 cases of intra-cranial aneurism in 5,432 post-mortems of the head—i.e., in 0.80 per cent. Busse² says that small aneurismal dilatations on the anterior communicating artery occur in as many as 10 per cent. of all post-mortem specimens. Intra-cranial aneurisms most frequently cause symptoms between the ages of 25 and 40, but may do so at any age.

* A Post-Graduate lecture delivered at the North Middlesex County Hospital on June 20th, 1934.

Subarachnoid hæmorrhage due to all causes is not at all rare. Its frequency is illustrated by the fact that over a period of eighteen months there were 24 cases at the Boston City Hospital and only 22 cases of subacute bacterial endocarditis, a much better known condition, over the same period.

I will begin by describing two cases which illustrate the usual history.

Case I.—Mrs. A.V.C., aged 37 years, was fairly well until August 17th, 1933, when she suddenly developed a very severe occipital headache and became stuporose. Two months previously she had undergone cæsarean section for nephritic toxæmia, but she recovered from this completely.

On admission to hospital shortly after the onset she was disorientated and restless. The findings were neck rigidity; no Kernig's sign; pupils, fundi and cranial nerves normal. B.P. 185/105. The urine contained a large amount of albumin. The C.S.F. was uniformly blood stained. After the lumbar puncture she became quiet and rational and gradually improved. On August 27th the C.S.F. was yellow and on September 2nd it was clear. On September 21st she suddenly again became comatose and the C.S.F. was once more blood stained. Next day she had a complete right third nerve paralysis and bilateral papilloedema with retinal hæmorrhages. She remained comatose and died on September 25th. W.R. Negative.

At autopsy there was a large subarachnoid hæmorrhage at the base of the brain and an aneurism the size of a pea at the junction of the right posterior cerebral and right posterior communicating arteries to which the third nerve was adherent. (Fig. 1.)

FIG. 1.

Case 1. Grenz ray photograph showing aneurism at junction of right middle cerebral and right posterior communicating arteries. The third nerve is adherent to the aneurism.

The next case shows certain additional features:—

Case II.—Mrs. M.M.A., aged 47 years, was admitted to hospital on October 27th, 1933. Two days previously she had sudden and severe headache with a transient loss of consciousness. On examination there were detected marked neck rigidity, partial right third nerve paralysis and many hæmorrhages in both discs, especially the right. The arms and legs were normal. The C.S.F. pressure was 250 mm. of C.S.F. and the fluid was uniformly bloodstained. On November 7th she developed a left hemiplegia and a large right subhyaloid hæmorrhage. She had delusions. On November 10th the C.S.F. was clear, but on November 15th, when she became comatose, it was bloodstained and she died on November 17th. W.R. Negative.

At autopsy hæmorrhage from an aneurism of the middle cerebral artery was found. The blood clot surrounded the right third nerve and extended into the right internal capsule.

Having described two characteristic cases I will now consider the chief points in diagnosis.

Most intracranial aneurisms are not diagnosed until they rupture. If the rupture is a large one flooding of the subarachnoid space with blood occurs and the picture of meningeal irritation of dramatically sudden onset appears. Headache is usually very intense and occipital, and stiffness of the neck is often marked. There are vomiting, giddiness and mental confusion or unconsciousness. Pyrexia is only moderate at first. If the hæmorrhage is extensive, coma, deepening until death, is usual. There is as a rule no paresis or other localising sign but transient and variable extensor plantar responses may be present. Focal signs may appear when the blood damages cranial nerves at the base of the brain or spreads into the brain substance. The two cases described above illustrate these features. The second case is an example of a crossed paralysis, but not quite the same as Weber's syndrome of third nerve paralysis on one side with hemiplegia on the opposite side. Weber's syndrome is due to a lesion in the crus cerebri and the third nerve palsy is nuclear and complete. In our case the third nerve palsy was incomplete since it was due to an infra-nuclear lesion of the nerve.

It must be remembered that the picture produced by an intracranial aneurism after a large rupture is simply that of spontaneous subarachnoid hæmorrhage, and although this condition has other causes it must be described in a consideration of intracranial aneurism. After rupture has occurred two procedures are helpful in arriving at a diagnosis:—

- (1) Ophthalmoscopy.
- (2) Lumbar puncture.

Ophthalmoscopy may reveal retinal and sub-hyaloid hæmorrhages and papilloedema. Riddoch and Goulden³ have shown that the hæmorrhages are due to blood in the sheath of the optic nerve causing obstruction of the central vein of the retina at the point where it leaves the optic nerve and crosses the sheath. The mechanism of their production is therefore the same as in increased intracranial pressure.

Lumbar puncture shortly after rupture will reveal blood which can be distinguished from blood due to the puncture itself by the fact that it is uniformly distributed in all samples and does not clot, and also by the fact that the supernatant fluid is yellowish. These features were first described by Froin⁴ in 1904.

Between the repeated bleedings of slow subarachnoid hæmorrhage and after non-fatal bleeding the C.S.F. may be very yellow and contain flakes of lymph. There is, however, no marked dissociation of cells and protein which would suggest a loculation syndrome.

I would emphasize two points concerning lumbar puncture in these cases. Firstly, it is important to realize that lumbar puncture may reveal almost pure blood. I have seen the diagnosis missed in a comatose patient because the blood was ascribed to accidental puncture of veins, and the fact that the spinal theca had been entered was not recognized. One of Symonds⁵ cases had a red blood cell count in the C.S.F. of over 3,000,000 per c.mm.

On the other hand, the concentration of red cells may be very low and the fluid may appear clear to the naked eye—probably because the initial hæmorrhage was small and clotting prevented the passage of blood in quantity into the spinal subarachnoid space. Such a case was described by Cookson.⁶

Secondly, the sudden onset of meningeal irritation and coma without localising signs and the finding of a bloody C.S.F. do not necessarily mean that the hæmorrhage is subarachnoid in origin, since the same picture may occur when a large intra-cerebral hæmorrhage ruptures into the ventricles (the cerebro-meningeal hæmorrhage of Froin) or on to the surface. In such cases complete suppression of tone and reflexes is present at first and there are no localising signs.

Symonds⁵ has pointed out that blood may reach the subarachnoid space by four routes:—

- (1) Rupture of a dural vein causing subdural and subarachnoid hæmorrhage.
- (2) Rupture through the pia of a superficial intra-cerebral hæmorrhage.
- (3) Rupture of a deep intra-cerebral hæmorrhage into the ventricle with extension of blood *via* the foramina of Magendie and Luschka into the subarachnoid space.
- (4) Rupture of a vessel or aneurism in the subarachnoid space itself.

Sometimes after a subarachnoid hæmorrhage albuminuria and glycosuria occur. Claude Bernard in his classic experiment demonstrated that puncture of the fourth ventricle produces an increased volume of urine and often albuminuria and glycosuria. Hæmorrhage in the region of the fourth ventricle has been known to produce glycosuria and it is possible that a similar mechanism is responsible in subarachnoid hæmorrhage.

Sometimes an aneurism may leak repeatedly and produce a very confusing picture. Slight signs of meningeal irritation may occur which may be mistaken for a simple stiff neck. Headache, aphasia, impairment of memory and perhaps cranial nerve palsies occur and occasionally encephalitis lethargica may be simulated. Korsakow's syndrome sometimes appears during recovery from subarachnoid hæmorrhage.

Signs of pressure on cranial nerves usually occur in these cases some days after the initial onset of symptoms, since the false aneurism formed by the blood clot is much larger than the original one.

Less frequently an aneurism may be diagnosed or suspected before rupture occurs because of signs of focal pressure involving one of the structures at the base of the brain as in the following case.

Case III.—Mrs. C.P., aged 59 years, was admitted to hospital with a left hemiplegia due to cerebral thrombosis, and towards the end of her illness it was noted that she had a partial right third nerve paralysis. At autopsy a cerebral thrombosis was found, and also an aneurism at the junction of the right middle cerebral and posterior communicating arteries to which the third nerve was adherent (Fig. 2.) It had not ruptured though it may have leaked a little without noticeable symptoms or signs beyond those due to involvement of the third nerve.

Other ante-mortem evidence of aneurism such as erosion of bone and calcification in the wall of the sac have been shown by the X-rays. Aneurisms have also been demonstrated by arterio-radiography. Sometimes a pulsating bruit has been heard.

FIG. II.

Case 3. Aneurism at the junction of the right middle cerebral and posterior communicating arteries. Slight leakage of blood causing adherence to third nerve.

It remains now to consider the ætiology and treatment of intra-cranial aneurisms.

Ætiology.

It is now known that many intra-cranial aneurisms are the result of congenital defects in the walls of the arteries, particularly at anastomotic junctions. The evidence for this view is strong. Aneurisms have been found in infants and may be associated with other congenital vascular abnormalities such as nævi and coarctation of the aorta. It is probably incorrect, however, to speak of "congenital" aneurisms since they are not congenital malformations in the ordinary sense. Wiley D. Forbus⁷ examined a case of multiple aneurisms of the circle of Willis and found, as other observers have done, that the walls of the aneurisms had no tunica media. He was able to demonstrate also that at the points of division of some cerebral vessels there were gaps in the media without aneurism formation. The defect in the tunica media constitutes a *locus minoris resistentiæ* in the vessel wall. The aneurism commonly called congenital should be regarded as an acquired lesion due to the combined effect of blood pressure and a congenital weakness of the vessel wall.

Syphilis plays little or no part in the ætiology of intra-cranial aneurism. This is what one would expect since, when syphilis affects the small arteries, it has a selective action on the intima and produces an obliterative type of endarteritis. It is only when it affects the media of the thoracic aorta that aneurism formation commonly results. Fearnside¹ estimated that while 96.2 per cent. of aneurisms of the aorta were due to syphilis only 6.25 per cent. of aneurisms of small arteries such as those of the circle of Willis were due to or associated with infection by the *Spirochæta pallida*.

Intra-cranial aneurisms may also be due to arterio-sclerosis and to embolism, and in rare instances to peri-arteritis acuta nodosa. In the last condition the cerebral vessels are seldom the only ones affected. Arterio-sclerotic aneurisms usually produce symptoms later in life than the "congenital" variety. Embolic or mycotic aneurisms occur usually in subacute bacterial endocarditis. The organisms in the embolus set up an acute arteritis which destroys the media with resultant aneurism formation.

It must be remembered that spontaneous subarachnoid hæmorrhage, as already mentioned, has other causes than aneurism. Thus in ten cases of spontaneous subarachnoid hæmorrhage, which I reported in 1932, six were fatal, but a ruptured aneurism was only found in one of these.⁸ Subarachnoid hæmorrhage in patients over 50 is more likely to be due to arteriosclerosis, with or without aneurism, than to the "congenital" variety of aneurism.

Treatment.

It is sometimes said that very little can be done for these cases, but a careful consideration of all the possibilities shows that a feeling of helplessness is by no means justified.

In embolic aneurisms the symptomatology and treatment are, as a rule, overshadowed by the primary condition.

Treatment of the "congenital" variety of aneurism is best considered under three headings:—

- (1) Before rupture.
- (2) Immediately after rupture.
- (3) During the stage of recovery.

In the rare cases in which an aneurism is diagnosed before it ruptures, the treatment is directed to the alleviation of symptoms and to measures calculated to

prevent any undue rise of blood pressure. Ligature of the internal carotid artery has been suggested.

The treatment after subarachnoid hæmorrhage occurs has been the subject of some controversy particularly with regard to lumbar puncture. This procedure is essential to establish the diagnosis and it may be repeated with benefit to the patient under certain conditions.

A useful summary is that given by Ingvar, quoted by Symonds,⁵ who recognises two stages. In the first, hæmorrhage is proceeding and the resulting rise of intra-cranial tension has a protective influence by reducing the rate of leakage. In this stage lumbar puncture should only be done to make the diagnosis and should only be repeated if the rise of intra-cranial pressure threatens life. In the second stage, when the hæmorrhage has ceased and the symptoms are due to a meningeal reaction, repeated lumbar puncture may be helpful. Ingvar recommends that the pressure of C.S.F. should never be reduced below 100 mm. of C.S.F.

It may not be an easy matter to decide when the intra-cranial conditions justify another lumbar puncture. We have to rely mainly on the general condition of the patient and on the blood pressure. The relationship between the blood pressure and the C.S.F. pressure is the subject of many contradictory observations. It is known that the pressure in the intra-cranial arteries rises and falls with that of the general intra-cranial pressure and that rises of intra-cranial pressure up to the diastolic blood pressure do not affect the blood pressure in the peripheral vessels. Hence the blood pressure in the brachial artery may be no guide to the blood pressure within the skull. It has been said that the C.S.F. pressure is always high when the blood pressure is high, but this relationship has been denied and it seems probable that it is only a sudden rise of blood pressure which affects the C.S.F. pressure.

The relationship between the pressures of blood and C.S.F. was well shown in case II. On admission to hospital the blood pressure was 170/110 mm. of Hg. Fourteen days later it had risen to 250/150 mm. The C.S.F. pressure was then 230 mm. of C.S.F., and removal of 12 cc. caused the blood pressure to fall at once to 150/110 mm.

In the present state of our knowledge we may say that lumbar puncture should be performed to make the diagnosis but should not be repeated while bleeding is going on, unless there is evidence of a dangerous rise of intra-cranial tension. Hyland¹⁰ recommends that the stylet should be adjusted so as to remove 20 c.cs. of fluid over a period of an hour, since the chance of causing a recurrence of bleeding is then diminished.

In addition to lumbar puncture other measures may be adopted as follows:—

- (1) To encourage coagulation of the blood.
Coagulen-Ciba may be given intramuscularly and also Calcium lævulinate (Tetanol. Crookes).
- (2) To reduce blood pressure.

Tight clothing round the neck should be removed, and the head placed so that return of blood from the skull is not impeded. Venesection may be advisable.

During the recovery stage the patient should be kept quiet on a non-stimulating diet. Coughing, straining at stool, exertion and emotion should be avoided and a careful watch should be kept on the blood pressure. Lumbar puncture may be performed to relieve headache and to remove the C.S.F. containing altered blood. Bagley's¹¹ work on animals indicates that blood in the C.S.F. is liable to cause meningeal adhesions and cortical damage and this is an additional argument in favour of lumbar puncture in the recovery stage.

Prognosis.

The prognosis of intra-cranial aneurism before rupture occurs is good, and after this accident it depends largely on the size of the hæmorrhage and whether the bleeding point is capable of firm closure or not. A large hæmorrhage may prove fatal without even temporary recovery. On the other hand, an aneurism may bleed several times and each hæmorrhage may be recovered from or one may be of fatal severity.

Ohler and Hurwitz⁹ published a group of 24 cases of subarachnoid hæmorrhage of all causes with a 50 per cent. mortality. They point out that the presence of associated diseases, especially of marked hypertension, adds considerably to the gravity of the prognosis.

In patients who survive rupture of an intra-cranial aneurism certain sequelæ may be noted. Headache may persist for a long period. There may be some reduction in mental function, but Korsakow's syndrome, when it occurs, usually disappears completely.

Hemiplegia will improve a little, but complete recovery is unlikely because some nervous tissue is destroyed by the extravasated blood. Some impairment of vision as a result of retinal hæmorrhage may be found. Hæmorrhage into the vitreous is usually completely absorbed, but occasionally organization results in retinitis proliferans.

The following are the details of a case of intra-cranial aneurism with partial recovery after rupture:—

Case IV.—Miss L.M.L., aged 19 years, works in a wireless factory. She has had no illnesses beyond measles and influenza and there is no history of head injury.

On January 6th, 1934, she developed a very sudden occipital headache, which rapidly improved after two days in bed. She went back to work until January 12th, but remembers nothing until she found herself in hospital on January 14th with severe headache and a completely closed left eye.

At this time she had a complete third nerve paralysis and papillœdema on the left side. The right eye was normal. Next day lumbar puncture revealed heavily blood-stained fluid. Four days later she gradually developed a right hemiplegia, which became complete in eight hours, and she later showed motor aphasia. Eleven days after admission to hospital the C.S.F. was as follows:—Pressure 190 mm. C.S.F.; clear and colourless; 20 cells per c.mm.; total protein 35 mgms. per cent.; sugar content normal.

W.R. negative (blood and C.S.F.). She has gradually improved and today shows a right hemi-paresis and a slight left ptosis. The aphasia is improving.

REFERENCES.

- (1) Fearnside, E. G., *Brain*, 1916, 39, 224.
- (2) Busse, O., *Virchow's Arch.*, 1921, 299, 178.
- (3) Goulden, C., and Riddoch, G., *Brit. Jour., Ophth.*, 1925, 9, 209.
- (4) Froin, *These de Paris*, 1904. Quoted by Symonds—see 5.
- (5) Symonds, C. P., *Quart. Jour. Med.*, 1924, 18, 93.
- (6) Cookson, H., *Brit. Med. Jour.*, 1933, 1, 555.
- (7) Forbus, Wiley D., *Bull. Johns Hopkins Hosp.*, 1930, 47, 239.
- (8) Birch, C. A., *Practitioner*, 1932, 129, 402.
- (9) Ohler, W. R., and Hurwitz, D., *Jour. Am. Med. Ass.*, 1932, 98, 1856.
- (10) Hyland, H. H., *Canad. Med. Ass. Jour.*, 1933, 29, 145.
- (11) Bagley, C., *Arch. Surg.*, 1928, 18, 18.