Observations on intracranial aneurysms. By R. W. Ross Russell. (From the Neurological Unit and Mallory Institute of Pathology, Boston City Hospital and the Department of Neurology, Harvard Medical School.) Brain 1963; 86: 425–442 with plates xxxvii–xl.

In the early 1960s, Ralph Ross Russell worked in Oxford with (Sir) George Pickering, whose principal interest at that time was the cause and effects of hypertension including what were then called ‘cerebral vascular accidents’ and which rested uneasily in a limbo between general medicine and neurology, attracting little attention from either. He recalls that Derek Denny-Brown, a former Rhodes scholar with (Sir Charles) Sherrington, visited the department and spoke on transient cerebral ischaemia, at that time attributed to vasospasm. Denny-Brown showed little evidence for this mechanism and proposed that a more likely cause was a localized reduction in the blood-flow to a compromised region of the brain due to a fall in systemic blood pressure. Pickering was delighted since he had spent years debunking vasospasm. Denny-Brown was then at the height of his powers. He had made immense contributions to neuroscience ranging from frontal lobe function to muscle fibre physiology. He was a dedicated ‘hands-on’ experimental worker but a hard taskmaster. It therefore came as something of a relief to Ralph Ross Russell that he was judged so ignorant of neuropathology that time must be spent at the Mallory Institute of the Boston City Hospital.

Ross Russell addressed an issue first identified by Johann Jacob Wepfer (Observationes anatomicae ex cadaveribus quos sustulit apoplexia, 1658) but still unresolved: what is the source of haemorrhage in cases where death is due to cerebral haemorrhage in the apparent absence of a ruptured major artery or vein? The predisposition for small vessels, especially perforating arteries of the basal ganglia, to be thickened and show degenerative changes had already been noted. In proposing that haemorrhage occurs from small saccular or fusiform arterial aneurysms, identified from water macerated vessels obtained at autopsy and measuring 250–400 μm in diameter, Jean-Martin Charcot and Henri Bouchard (Nouvelles recherches sur la pathogenie de l’hémmorragie cérébrale. Arch Physiol Norm Pathol 1: 110 et seq.; 643 et seq. and 725 et seq.) concluded that such changes are the result of periarteritis and, despite the clear association with systemic hypertension, have nothing to do with atheroma (Fig. 1). Professor A. G. Ellis had already found microscopic aneurysms in many such cases (A. G. Ellis. Proc Pathol Soc Philad 1909; 12: 197 et seq.). Some showed continuity between the perivascular haematoma and intramural contents of the vessel, apparently through intimal rupture and subsequent degeneration of the media. But Ellis’s work had been interpreted as indicating that miliary aneurysms are in fact periadventitial haematomas. Others came at the problem from the opposite direction concluding that aneurysms are a secondary phenomenon, haemorrhage occurring within existing areas of perivascular brain autolysis resulting from the action of enzymes delivered through the systemic circulation. Favouring Charcot and Bouchard’s position on the matter, Dr Ross Russell set out to confirm the presence of miliary aneurysms as the primary event in intracerebral haemorrhage using the technique of arteriolar X-ray micro-angiography.

Access to a resource of ~1300 autopsies performed annually on patients admitted to the 1500 bed Boston City Hospital allowed Dr Ross Russell to examine two brains each week within 24 h of death over a 7 month period. Cases were unselected apart from the exclusion of patients aged <20 years, diabetics and those with neurological disorders other than cerebrovascular disease (10 of 54 cases). Prior hypertension, present in 16 (30%) individuals, was registered if the initial diastolic recording on hospital admission was ≥110 mmHg. The preparation of specimens involved immediate perfusion of the carotid arteries with barium sulphate in gelatine, followed by cooling and formalin fixation of the brains for 2 weeks. Then, 0.6 cm slices were X-rayed with resolution for aneurysms having a calibre of ≥30 μm; later, the sections were dehydrated and examined histologically. Ralph Ross Russell reports on normal and pathological appearances of the striate vasculature and vessels that penetrate the cerebral grey and white matter.

The larger striate vessels (diameter 200–400 μm) branch in the putamen before ending in the body of the caudate nucleus: one artery traverses the internal capsule; more medial vessels supply the outer segment of the globus pallidus; the inner part and the inferomedial portion of the head of the caudate nucleus are supplied by branches of the anterior choroidal artery; and the thalamus receives its vascular supply from the basilar artery via the posterior cerebral vessels. In the main, these are end-arteries with few anastomoses. Conversely, the cortical arteries penetrate and turn to reach the periventricular region providing anastomoses between the pial vasculature, branches of the anterior and middle cerebral arteries, and the striate vessels.

As expected, age takes its toll on the striate vasculature, the vessels becoming tortuous, or even coiled to resemble aneurysms, and elongated even in normotensive individuals.
Hypertensive arteries are characterized by atheromatous degeneration, with variations in calibre of the lumen—especially at points of bifurcation where the angle taken becomes less acute and somewhat straightened—and some fusiform dilatations. But the main finding is the high frequency of aneurysms. This affects all individuals considered to be hypertensive, and 26 of 54 in the total series. Up to 20 aneurysms might be present in any one individual. These are concentrated in the putamen, pallidum, thalamus, caudate nucleus, internal capsule, centrum semiovale and cortical grey matter (Fig. 2). Multiple aneurysms occur only in hypertensives, and not at <50 years of age. Their intima may be thickened: the elastic lamina is reduplicated or frayed; the muscular layer is attenuated; and the adventitia usually normal. Characteristically, aneurysms arise at bifurcation points of branches where the media ends abruptly and the elastic layer extends a variable distance into the aneurysm; its wall consists only of intima, contiguous with the parent vessel and its adventitia. Histological evidence for haemorrhage and sequential thrombosis is apparent.

These observations suggest a mechanism whereby high intraluminal pressure and weakness in the arterial wall rupture the elastic lamina, distending the remaining wall made up of muscular elements and connective tissue (Fig. 3). The intimal connective tissue proliferates, producing hyaline appearances on the luminal surface and collagenous changes in the deeper layers. Bleeding occurs through the ruptured endothelium, and there are astrocyte and macrophage (microglial) reactions in the surrounding tissue. Many aneurysms thrombose, but new lesions form along the parent vessel. Finally, Dr Ross Russell debates the issue of whether—given their independent associations with hypertension—anurysm...
formation and intracranial haemorrhage are directly related, as Charcot had proposed. His evidence refutes the suggestions that aneurysms are nothing more than perivascular haematomas and haemorrhage always precedes aneurysm formation—the converse evidently being the case. A useful distinction can be drawn between true and false aneurysms, although each are vascular dilatations in continuity with the blood stream. But it was not so easy to prove that massive cerebral bleeding is always due to rupture of miliary aneurysms since, if true, the responsible lesion may be destroyed in the process of bleeding. Ross Russell felt able to conclude that: ‘age and hypertension produce a degeneration of muscular and elastic elements of small cerebral arteries which goes on to the formation of miliary aneurysms especially in the basal ganglia. The aneurysms frequently show evidence of minor haemorrhage and can be shown to be points of least resistance in the arterial wall. Soon after the initial rupture of the elastic lamina and before the stage of intimal thickening there is an increased tendency for massive haemorrhage’.

Forty-two years later, Ralph Ross Russell acknowledges that whether or not massive cerebral haemorrhage originates from the rupture of microaneurysms is still uncertain because of the distortion and secondary effects of the haematoma. But there seems little doubt that structural changes found in the walls of microaneurysms are very similar to those of lipohyalinosis described by C. Miller Fisher are now widely accepted as the cause of lacunar infarction. The hyaline and fatty material that Dr Fisher found may, in fact, be insudation of plasma through the weakened walls of the aneurysms that were so prevalent in the brains of hypertensive Bostonians studied at the instigation of Derek Denny-Brown by Ralph Ross Russell in the 1960s.

Alastair Compston
Cambridge