The Effects of Hypertension on the Nervous System*

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ABSTRACT

With 60 million Americans meeting criteria for either essential or secondary hypertension, elevated arterial pressures remain a major health problem. While efforts to find etiologies for essential hypertension continue, clinicians battle its effects on organ systems, including the nervous system. Hypertensive changes in the nervous system may be acute, chronic, or both. The intracerebral vasculature is commonly affected. Not infrequently, acute changes including hemorrhage, encephalopathy, and cerebral edema are superimposed on chronic changes of hyaline and fibrinoid arteriolosclerosis. Chronic vascular changes sacrifice vascular lumina. The resulting ischemia is responsible for cystic (lacunar) lesions and subcortical ischemic white matter lesions consistent with Binswanger's disease.

Introduction

Elevated systemic arterial pressure continues to be a devastating public health problem. In spite of decreasing U.S. cardiovascular mortalities, the contribution of hypertension to vascular disease throughout the body remains significant. Hypertension is currently the most common reason for office visits to physicians in the U.S. As many as 60 million Americans have blood pressures above 140/90 mmHg. Blacks appear to have a higher incidence and apparently are more susceptible to complications and end organ damage. Since most individuals with hypertension are asymptomatic, these patients may remain oblivious to their elevated blood pressures. Detection becomes critical since undetected or untreated hypertension often leads to lethal complications.

The World Health Organization defines hypertension at pressures greater than 160/90 torr, while most U.S. authors consider 140/90 adequate criteria. Assessing hypertensive patients on an individual basis rather than by strict numerical analysis is mandatory since average blood pressures increase with age. An 80-year-old could easily have systolic pressures approaching 170. Against this somewhat ambiguous criterion defining hypertension, categories of essential (primary) and secondary hypertension are described.
Ninety-five percent of all patients with elevated arterial pressures lack an identifiable cause thus suffering idiopathic hypertension, also known as essential or primary hypertension. The remaining five percent of hypertensive individuals have secondary hypertension with recognized etiologies for their elevated blood pressures. Both essential and secondary hypertension are described further as either “benign” or “malignant” based on clinical course. In most instances, hypertension is stable and is compatible with long life. This “benign” hypertension lacks the aggressiveness of rapidly progressing “malignant” hypertension characterized by extraordinarily high pressures and, if untreated, relatively short survival periods.1,8,11

Further efforts to categorize hypertension have developed “degrees” including; mild (diastolic 90 to 104mmHg), moderate (diastolic 105 to 114mmHg), and severe (diastolic > 115mmHg).1 These continuing attempts to define hypertension may be a result of an inability to find a specific pathophysiologic mechanism to explain essential hypertension. With arterial pressures dependent on cardiac output and peripheral resistance, secondary hypertension is generally due to underlying disorders that contribute to these variables. Blood volume, humoral mediators causing arterial constriction and dilatation, and cardiac factors of rate and contractility, all contribute to baseline arterial pressures.

Secondary hypertension is often related to renal mechanisms. With the kidney participating in blood volume control and peripheral resistance, disorders of the renin-angiotensin system, renal artery stenosis, or errors in sodium regulation/excretion are frequently implicated. Other identifiable sources of secondary hypertension include endocrine disorders such as Cushing, Conn, and pheochromocytoma syndromes. Vascular lesions of aortic coarctation and pol- yarteritis are rare causes, while neurogenic sources of hypertension include increased intracranial pressure (Cushing reflex) and the poorly understood psychogenic origins.1,8,11

Most hypotheses for essential hypertension implicate genetic and environmental derangements that result in some abnormality between the controlling mechanisms of cardiac output, renal function, peripheral resistance, and sodium homeostasis.11 Essential hypertension seems to involve an increased vascular resistance from expanded vascular volume. This increased volume is likely due to renal sodium retention resulting in an associated increased cardiac output. Other theories suggest an inherited defect impeding sodium transfer across cellular membranes. The secondarily increased sodium and calcium concentrations may result in increased vascular tone and reactivity of circulatory vessels.14 Intrarenal humoral mechanisms may also contribute to essential hypertension.

Assuming pressure related naturiesis provides a central role in pressure regulation, humoral systems within the kidney that control hemodynamics are becoming promising areas of research. Renal humoral factors, prostaglandin I2 and endothelial relaxing factor, modulate autoregulatory control of afferent arteries which in turn affect release of renin from the juxtaglomerular apparatus. Another intrarenal humoral factor, prostaglandin E2, may have direct effects on sodium excretion by its actions on tubular resorption. Romero et al suggest variations in the medullary prostaglandins and relaxing factors contribute to hypertension and may be the initiating events of essential hypertension.9,10,14

Regardless of etiology, the effects of hypertension on the nervous system and its vasculature can be severe, manifesting as chronic or devastatingly acute changes. Commonly, hypertensive
patients suffer longstanding chronic changes with superimposed acute alterations (table I).

**Acute Hypertensive Changes**

As the origins of hypertension unfold, clinicians continue to battle the widespread and unsparing effects of hypertension on multiple organ systems. The single most important risk factor in cerebral vascular disease is hypertension. Pathologic changes owing to hypertension in the central nervous system (CNS) can be categorized as acute or chronic. These include hemorrhages, hyaline and fibrinoid arterial and arteriolar sclerosis, atheroma formation, lacunae, hypertensive encephalopathy, and Binswanger's disease. Acute hypertensive changes in the nervous system are illustrated by the following patient.

**Case History**

G.S., a 41-year-old black male, was brought to the emergency room of Truman Medical Center, Kansas City, MO, by ambulance after he apparently ordered his son to dial 911. Paramedics found him trembling with rigid extremities. On admission, he was conscious but aphasic, with reactive pupils 3mm in size. Blood pressure was 250/180mm Hg. Efforts to control pressures and medical management were initiated. Despite medical efforts, the patient continued to deteriorate, requiring mechanical ventilation. A CAT scan revealed a large intraventricular and intraparenchymal hemorrhage involving the cerebellar vermis. G.S. received an intraventricular drain in the operating room. Postoperatively, cardiac arrest occurred and the patient was successfully resuscitated. EEG's were performed, and brain death was confirmed two days postoperatively.

Autopsy findings revealed myocardial hypertrophy, cystic medial necrosis of the aorta, and diffuse arteriosclerotic disease with nephrosclerosis—all consistent with longstanding hypertension. Major postmortem findings showed extensive hemorrhage into the fourth ventricle and pons with massive destruction of brain tissue. Acute expansion of the hemorrhage displaced the midbrain upward. Evidence of increased intracranial pressure with resultant herniation of several structures including the brainstem were found.

Intracranial hemorrhage (figure 1) is the most devastating of acute hypertensive changes in the CNS. While several spontaneous intracranial hemorrhages are recognized, only "intracerebral" hemorrhages are associated with hypertension. Subarachnoid hemorrhage and bleeding from vascular malformations are only weakly associated with concurrent hypertension. As in the case described, most intracerebral hemorrhages are associated with hypertension and are thought to result from ruptured "Charcot-Bouchard" microaneurysms. These result from increased arterial pressure in small intraparenchymal arteries and are often seen with fibrinoid necrosis in adjacent arteries and arterioles. Charcot-Bouchard aneurysms must not be confused with berry aneurysms which occur at branching sites of major extraparenchymal (subarachnoid) arteries. Berry aneurysmal rupture results in subarachnoid hemorrhage and is generally not associated with hypertension.

The role for hypertension in intracerebral bleeding from vascular malformations remains in question. During proton radiation therapy, the average systolic and diastolic pressures increase over 30mmHg. Szabo cites 56 patients receiving proton radiation therapy without a single case of bleeding from vascular malformations during the increase in arterial pressure. Szabo's study supports the thought that paroxysmal hypertension plays little if any role in bleeding from vascular malformations.

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**TABLE I**

Hypertensive Changes in the Brain

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<thead>
<tr>
<th>Acute</th>
<th>Chronic</th>
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<tr>
<td>(1) Encephalopathy with cerebral edema</td>
<td>(1) Arterial and arteriolar sclerosis, atherosclerotic, and lipohyalinosis</td>
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<tr>
<td>(2) Fibrinoid arteriolar sclerosis</td>
<td>(2) Charcot-Bouchard aneurysm</td>
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<td>(3) Intraparenchymal hemorrhages</td>
<td>(3) Infarcts and lacunes</td>
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<td>(4) Subcortical leukoencephalopathy</td>
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<td><em>(Binswanger’s disease)</em></td>
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to forced vasodilatation resulting in autoregulatory breakdown.\textsuperscript{5} Such extreme increases in pressures necessary for forced vasodilation are seen in hypertension secondary to acute glomerulonephritis, toxemia of pregnancy, and idiopathic malignant hypertension. Characterized by increased flow, symptoms of hypertensive encephalopathy include headache, depressed alertness and intellectual function, vomiting, and convulsions.\textsuperscript{6,13} Although the neurologic features of hypertensive encephalopathy can be reversed by lowering the blood pressures, untreated or malignant progression causes fibrinoid necrosis and thrombosis of cerebral arterioles with microinfarcts. Petechial hemorrhages and associated cerebral edema quickly follow. With uncontrolled increasing blood pressure, cerebral edema may lead to coma and death.\textsuperscript{6,8,13}

Chronic Hypertensive Changes

Changes within the CNS owing to chronic hypertension are illustrated by the following patient.

Case History

C.P. was a 78-year-old black female with longstanding hypertension who was brought to Truman Medical Center, Kansas City, MO, by ambulance after she had been found lying on her floor at home unable to get up owing to left sided weakness. After admission, her condition stabilized. One week later, she was transferred to another institution for therapy and rehabilitation. Her condition progressed satisfactorily until approximately one month after transfer when she suddenly became unresponsive with labored respirations. EKG showed an anterior wall myocardial infarction. Resuscitation was unsuccessful and the patient was pronounced dead.

Autopsy revealed diffuse vascular disease including atherosclerosis of the aorta and coronary arteries, left ventricular hypertrophy, and arteriosclerosis. Numerous bilateral ischemic lesions throughout the subcortical white matter consistent withBinswanger's disease ranged from 1.0cm to microscopic. Some of these infarcted areas had undergone cystic (lacunar) degeneration. Consis-
EFFECTS OF HYPERTENSION ON THE NERVOUS SYSTEM

Few organs are spared by longstanding hypertension. Kidney, heart, vessels, and brain are common targets. The previous patient illustrates several chronic changes seen in the cerebral vasculature and parenchyma of hypertensive patients. Hypertensive vascular disease is the most common chronic change seen in the central nervous system. While hypertensive changes spare veins, arterial vessels show accelerated arteriosclerosis with hyalinosis, fibrosis, and altered brain capillaries. The central lesion is the reduced lumina of arteries and arterioles. Hypertension causes small muscular arteries to suffer segmental dilatation resulting from smooth muscle necrosis. Endothelial integrity is lost causing increased permeability to fibrin and plasma proteins. This cell necrosis with protein deposition produces fibrinoid necrosis which is quickly followed by smooth muscle proliferation, yielding the "onion-skin" appearance with reduced vascular lumens. This type of hypertensive injury and repair has been labeled "malignant arteriolosclerosis" and is seen more often in patients with quite high blood pressures.8,11

Patients suffering benign hypertension have a more chronic course with thickened vessel walls owing to deposition of collagen and plasma protein. Termed "benign arteriolosclerosis," this hyalinization of blood vessels is thought to be due to hypertension as well as aging.8,11 Increased vascular hyalinization with aging may be secondary to increased pressures in older individuals.

Hypertension accelerates lipid accumulation in vessel walls, so that atheroma formation, particularly in larger cerebral vessels, is increased. This accelerated arteriosclerosis potentially leads to cortical and subcortical infarcts. While normotensive patients rarely suffer atheroma formation in vessels less than 0.2cm, chronically hypertensive patients have atheromas involving smaller vessels like those supplying critical areas of the internal capsule, basal ganglia, and pons.5 Cerebral infarction occurs where blood flow decreases below the metabolic needs of parenchymal tissue. The middle cerebral artery and its branches are most often involved.8

Vascular lesions predominate as the most common chronic hypertensive change in the CNS. Lacunae, which are commonly found in hypertensive patients, are cystic lesions ranging from two to 15mm.5 Found in deep portions of the brain, lacunae have favored locations including lentiform nucleus, caudate nucleus, thalamus, and internal capsule. Hypertensive vascular changes contribute to lacunar formation and cortical infarction. Lacunae may result from infarcts owing to lipid and hyaline deposition in vessels—so called lipophyalinosis.4 Less frequently, lacunae result from small hemorrhages. They remain asymptomatic unless strategically located.4,5

Perhaps the most significant findings in the brain of our patient were the numerous ischemic areas in the subcortical white matter consistent with "leukoaraiosis" and characteristic ofBinswanger's disease. This white matter atrophy was first described by Otto Binswanger in 1894 and is seen in hypertensive and demented patients. The major pathologic feature of subcortical arteriosclerotic encephalopathy (Binswanger's disease) which distinguishes it from other cerebral vascular disease is the regional loss of white matter with associated gliosis.2,3 These white matter changes exhibit diffuse and irregular loss of myelin and axons. Often seen concurrently, arteriolar sclerosis of the locally penetrating arteries suggests an ischemic cause.8 Severe sclerosis from longstanding hypertension may result in decreased perfusion during occasional periods of
hypotension. Pre-existing hypertension with atherosclerotic disease nearly always coexists with Binswanger's disease.³

References


