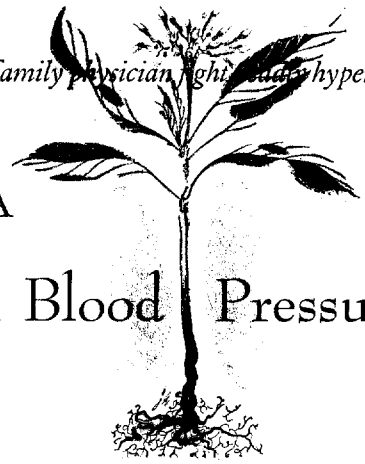
A new chemical weapon helps the family physician fight sudden hypertension



RAUWOLFIA
Against High Blood Pressure

By Paul de Kruif

OF COURSE high blood pressure can be harmless; many people live a normal life span unaware they have this condition. And yet a fifth of all death is directly or indirectly due to the results of hypertension. Against this death there is now definite chemical hope. An ancient, mysterious drug from India is helping make successful treatment of severe hypertension possible for general practitioners.

If so many can live years not knowing they're hypertensive, how can doctors be sure a given case is dangerous? They can't, but they have clues. It's more likely to be serious when it runs in families or starts early in grownup life.

Serious hypertension starts insidiously; only a minority of its victims have symptoms (notably fatigue) that send them to their doctors. Most high blood pressure is stumbled upon at insurance, blood-donor or routine medical examinations. Hypertension in itself isn't a disease. An ominous figure — let's say, 220/120 — simply measures the pressure in the arteries: the first of the figures, *systolic* pressure, when the heart's pumping; the second, *diastolic* pressure, when the heart's relaxing. Diastolic is as low as the pressure goes; and, if that's high for one's age, then there may be disaster. But why?

The heart has to pump harder against a chronic rising blood pressure until at last its muscle may fail. And when the pressure stays high for years, it aggravates thickening and deterioration of arteries. If the heart arteries plug up, there is a coronary accident; if the brain arteries plug or burst, there is a stroke; and damage to kidney arteries may result in fatal uremia.

This sinister trinity of hypertensive disease of blood vessels of the heart, brain or kidneys is the king killer — responsible for the death of 320,000 Americans yearly.

What is it that makes blood pres-

sure go up dangerously? It used to be thought it began with a hardening and plugging of arteries; it was believed especially prevalent in overweight people. But now it is known that the great majority of cases start from deranged nerve activity causing chronic spasm of the blood vessels. Overactive impulses go from deep in the brain out over the sympathetic nervous system, which, independently of our will, controls organs, glands and blood vessels.

The overactive sympathetic nerve impulses narrow down the little valves at the ends of the arteries; so the heart must pump harder to circulate the blood, thus shooting up the pressure.

If the sympathetic nervous system is to blame, why not cut its nerves, blocking overactive impulses? That was the bold question asked by the late great Dr. Max Minor Peet of the University of Michigan. He risked the operation on a patient terribly hypertensive and given up to die. The man's pressure dropped to normal. In good health again, he worked many years — outliving the doctor who had saved his life.

Dr. Peet's now famous sympathectomy operation — perfected by Dr. Reginald Smithwick of Boston and Dr. Keith Grimson of Durham, N. C. — has saved thousands of hypertensives who were doomed to early death. Yet sympathectomy, though often lifesaving, could not be the answer. For millions of not yet desperately ill hypertensives the operation seemed too risky. Many wouldn't face it; they preferred to take their chances with high blood pressure.

But now that we are in the age of chemistry, scientists asked, why the knife? Surely there must be some chemical that would block the overactive sympathetic nervous system? And British searchers, W. D. Paton and E. G. Zaimis, came up with a synthetic agent, hexamethonium. It sensationally knocked terrific blood pressures down to normal. And from Ciba laboratories in Switzerland came hydralazine, commonly known as Apresoline. This, too, was promising.

In 1950 Dr. Edward D. Freis, in Washington, D. C., and Dr. Henry A. Schroeder, in St. Louis, tried combining hexamethonium and hydralazine in a double-barreled assault on hypertension. They were bold. At first they picked only those hypertensions classed as malignant: hemorrhages into the retinas of the patients' eyes dimmed their vision; they had excruciating headaches and dizziness to the point of coma; they were in constant peril of strokes and of failure of their overburdened hearts; they were in danger of fatal uremia.

Why did Freis and Schroeder test this new treatment first on cases of malignant hypertension — cases doomed to death perhaps within a year? Because the treatment also was drastic. Hexamethonium was so powerful that it drove high blood pressure down until patients went dizzy, often passing out,

falling on their faces. Hydralazine caused severe headaches and fast pounding of hearts already likely to be damaged.

With death the alternative, they decided to risk the hexamethonium-hydralazine treatment. Out of 100 malignant hypertensives thus treated by Dr. Schroeder 63 have survived from one to two years, 57 of them back working. Blood pressure? Back practically to normal. No further damage to their hearts or brains or even their kidneys. Dr. Freis's results were similar.

It was historic. For the first time, malignant hypertension was stopped, chemically. But then came word of how these resurrected lived under a sword. Eleven patients stopped the treatment; within a few weeks all were dead.

If only they'd stuck with it! But sometimes it was too tough to take. Hexamethonium-hydralazine was practical for patients in hospitals and under close supervision of experts; for many it was too high a price to pay for living; and it was hardly the medicine for busy family doctors to use on hypertensives generally.

Now arose Rauwolfia, the powdered root of a humble shrub from India. It had long been medically advertised in ten Oriental languages as a remedy for mild and severe insanities, hysteria and epileptic fits; for hundreds of years it had been popularly supposed to be fine for fevers, different diarrheas and snake bites. It is reliably reported that Mahatma Gandhi, by chewing on this Rauwolfia root, increased the calm that helped him defy the might of the British Empire.

In 1950 Dr. Robert Wilkins of Boston read an article by Hindu Dr. Rustom Jal Vakil, who said Rauwolfia was pretty good for hypertension, too. Crazy though the Oriental claims for it seemed to be, Wilkins decided just to try it on hypertensives. He gave it in single trial doses. Nothing happened. Wilkins very nearly threw Rauwolfia out the window. But then a seriously hypertensive woman was given the Indian medicine six days in succession and on the sixth day her pressure was way down.

What Dr. Wilkins now found was strange. Contrary to the other chemicals that had been tried, Rauwolfia was gentle, took days to show any effect on blood pressure at all. It was far from a wonder drug; it lowered blood pressure only modestly; it brought only 13 of Wilkins's first 39 cases down to normal.

It developed that Rauwolfia made up for its modest lowering of pressure by an amazing effect on symptoms: it was a tranquilizer; it soothed headaches and dizziness; picked butterflies out of stomachs of anxious neurotics; calmed high-powered hypertensives who drove not only themselves but all around them — and their own blood pressure up to boot.

Rauwolfia had another weird quality. It tamed the bad effects of the other drugs that Wilkins and his

co-workers — Drs. Walter Judson, William Hollander and Meyer Halperin — had to use to treat severe hypertension. It slowed down the fast-pounding hearts caused by hydralazine. It made the use of another drug, veratrum, more practical. Though lowering blood pressure, veratrum had also made victims vomit. Rauwolfia made it possible to cut down the veratrum dose, thereby preventing nausea.

Rauwolfia's own side-effects were trivial. Stuffy nose, increased dreams, overactive elimination. These effects are generally controllable by cutting Rauwolfia down to smaller, but still effective, doses.

This eerie medicine transformed long-suffering hypertensives. Many told Wilkins: "I've *never* felt so well," or "This is how I *dreamed* of feeling," or "*Nothing* bothers me."

Yet Rauwolfia, even when combined with hydralazine or veratrum or both, failed to help every severe hypertensive. Could the gentle Indian medicine tame wild, powerful hexamethonium and so bring practical help to these hopeless patients?

Having got a new Rauwolfia extract (Rauwiloid) from Riker Laboratories, Dr. John H. Moyer, of Baylor University College of Medicine, Houston, Texas, tried it on a 47-year-old woman who was having a grim time trying to stay alive on hexamethonium alone. A year before, that big dangerous chemical cannon had rescued her when she was in a coma, about to die, blood pressure: 300/200! Her pressure plummeted to 140/90, normal. But then it went way below normal; the hexamethonium that had saved her life sent her into another ordeal. Often her pressure was so low her blood couldn't get to her head when she stood up, causing total blackouts. For a year she lived under this threat in order to stay alive at all.

Now Moyer added Rauwolfia. Her pressure steadied. Soon she needed only half her former dose of hexamethonium to keep it near normal. Then, no hexamethonium at all. Just Rauwolfia, a few tablets daily. I've never seen a woman more serene, healthy, lovely — three years after she should have died.

Moyer and his co-workers — Drs. R. V. Ford, W. R. Livesay and S. I. Miller — have brought 27 surely doomed people out of hypertensive crises by combined Rauwolfia-hexamethonium. They've had failures, too, going out of control and dying. But they've seen something highly significant while saving those 27 lives:

When truly severe high blood pressure is safely lowered by this double-barreled attack, then laboratory tests give evidence of arrest and often an actual reversal of deadly deterioration of the arteries of the heart, eyes and brain.

At the Jefferson Davis hypertension clinic in Houston Dr. Moyer and his young associates — Drs. Edward Dennis, Warren Hughes, Robert McConn and Liston Beazley — are searching for practical ways to

help general practitioners fight severe hypertension, chemically. Their patients are poor and are poor risks. Some lucky people may beat their dangerous hypertension down by a nice long rest in hospital or by going on an ocean voyage. But patients at the JD clinic couldn't afford either. The only hope was chemical. The doctors started with Rauwolfia.

Moyer's young doctors were anxious for me to understand that their battle against severe hypertension was not miraculous. There were people who couldn't take the treatment; who lapsed it; or whose blood pressure went out of control.

But the patients they did succeed in helping thought what happened to them was really something. An old Negro woman drying her tears on a bedraggled painted scarf said she was crying because it was wonderful how this medicine kept her working. Another explained how easy it was now to take care of the three children she served as Mammy. The doctors? "They're nice, oh, they're nice!"

At the JD clinic, crowded with 200 hypertensives, the faces of many reveal a new, curious, chemical serenity. Why not? Dr. Moyer reports that the chemical treatment significantly lowers high blood pressure in nine out of every ten; that it brings it down to normal in nearly half; and seven out of every ten who've been seriously sick become so well that they can again earn their living.

There's a hint of an even greater place for humble Rauwolfia — the strong possibility that it may give general practitioners a chance to do what only they can do best. *They may be able to prevent mild hypertension from becoming serious.*

For hypertension has this weakness: it usually fools around years before becoming sinister. Dr. George A. Perera, of New York City, followed the fate of 100 hypertensives whose condition began when they were young, average age 32. Their high blood pressure lasted on the average nearly 20 years before it was terminated — by death.

Rauwolfia's deep promise is the possibility that it may control high blood pressure serious from the start. Dr. Wilkins reports a number of such cases: one young man, for example, whose blood pressure — 180/120 — kept him out of the Air Force. His heart showed beginning damage. But now, for three years, one little daily dose of Rauwolfia has kept him husky, blood pressure a low normal; and the bad heart signs have gone.

Dr. Moyer reports a group of very early mild hypertensives kept on Rauwolfia for more than a year, with 63 percent responding. Rarely and briefly among these the blood pressure has risen above the gentle medicine's complete control. Even in early but moderately severe hypertensives, responding initially, Rauwolfia has kept blood pressure normal in 40 out of 50; and in the rest it's quickly and easily brought back within bounds by adding safe mod-

erate doses of hydralazine, veratrum or hexamethonium.

Less than five years ago there was great argument whether physicians, discovering a high blood pressure, should tell patients about it. Telling them might scare the pressure higher. Such mystification is superfluous now that there are reliable ways to keep early hypertension down.

Nationwide, hundreds of thousands of hypertensives are being treated with Rauwolfia. In active medical centers all over the country it's by far the most commonly used drug for the treatment of hypertension — because of its safety and its calming action, both on patients and on more powerful drugs. Nearly every physician treating hypertension has already used it.

Rauwolfia is now available in pure crystals, Serpasil, produced by Dr. Emil Schittler of Ciba laboratories. The crystals permit smaller doses, but the crude root (Raudixin) may hide undiscovered Rauwolfia virtues.

The cost? Only about 20 cents a day to keep hypertension down. And the tremendous demand, boosting production, will surely bring the price down further. Meanwhile, it's wise to treat hypertension early, for the cost of treating it later, when it's severe, runs to $1.50 daily; and, in hospital, a lot more than that.

A new chemical is now ready to aid Rauwolfia in severe cases. Pyrollidinium is more potent than hexamethonium and longer-acting and less violent, according to Drs. Freis and Moyer.

"Less than five years ago when we were asked to lower serious hypertension with drugs, we had nothing to offer," says Dr. Wilkins. "Now no case can be called impossible to treat until so proved."