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# History of hypertension

HISTORICAL HYPERTENSION RECORDED BACK AS 2600 B.C. HOLD MENTION AS "HARD PULSE DISEASE"

1ST TREATMENT: LEECHING, PHLEBOTOMY, ACUPUNCTURE

HIPPOCRATES RECOMMENDED PHLEBOTOMY

120 AD-COPPING OF SPINE TO DROW ANIMAL SPIRIT DOWN & OUT WAS RECOMMENDED

The history of hypertension goes back a long way. In ancient Chinese • and Indian Ayurvedic medicine, the quality of an individual's pulse, as felt by gentle palpation by the trained physician, was a window into the condition of the cardiovascular system. What was called "hard pulse" possibly would qualify for the modern term of hypertension.

Any article on the history of hypertension, however, is incomplete • without a mention of Akbar Mahomed's contribution in developing the modern concept of hypertension. In the late nineteenth century, Frederick Akbar Mahomed (1849–1884), an Irish-Indian physician working at Guy's hospital in London, first described conditions that later came to be known as “essential hypertension,” separating it from the similar vascular changes seen in chronic glomerulonephritis such as Bright's disease. Some of the noteworthy contributions of Akbar Mahomed were the demonstration that high BP could exist in apparently healthy individuals, that high BP was more likely in older populations, and that the heart, kidneys, and brain could be affected by high arterial tension

However, only with the advent of the mercury sphygmomanometer in the early twentieth century and defining of the systolic and diastolic BP by appearance/disappearance of Korotkoff sounds as heard *via* the stethoscope, the modern quantitative concept of hypertension , broken into systolic and diastolic categories – came into existence. By the middle of the twentieth century, checking BP by sphygmomanometer became part of the routine physical examination in hospitals and clinics

Hypertension, however, was not always considered a disease as we know it now. President Franklin D. Roosevelt was given a clean bill of health by his physician even when his BP was recorded as ~220/120. A few years later while at Yalta, Winston Churchill's personal physician noted in his diary that President Roosevelt "appeared to be have had signs of 'hardening of the arteries disease' and had a few months to live." Subsequent events demonstrated the truth of his diagnosis. President Roosevelt ultimately had a fatal hemorrhagic stroke 2 months later, and his death (1945)brought hypertension's potential as a deadly malady to the lime light

Yet, throughout the 1960s, the debate continued in the medical community regarding whether a need existed for treating the common variety of hypertension, by then aptly named “essential hypertension” because it was deemed an unavoidable, hence essential, component of the aging process. Attempts to treat hypertension, with the few drugs that were available at the time, often caused more misery and earlier demise for the patients than leaving them untreated

ESSENTIAL DEFINITION: **ABSOLUTLY NECESSARY EXTREMELY IMPORTANT**

The prevailing attitude in the academic community was expressed in an editorial in the Archive of Internal medicine in 1965 by two professors of medicine from New York.

To quote

*It is common experience that many patients live medically uneventful lives in spite of prolonged and considerable blood pressure elevation. In our study group's experience with 241 living and continuously employed hypertensive patients, followed from 10–25 years, a so called benign course was the rule, not the exception ... A drug that will maintain BP in the normal range in the supine as well as upright position without adverse physiological effects for all 24 hours over a period of years, when and if available, may well make medical history*

*One needs only to look back at the past 50 years to be amazed and deeply concerned at the worldwide enthusiasm generated by many proposed therapies for hypertension which eventually met their deserved doom – oblivion*



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To quote

*Acceptable techniques for obtaining the necessary proof are presently not available. We believe that critical techniques designed for a more precise and scientific answer to the problem under discussion will appear much sooner in an atmosphere of less enthusiasm and more caution in interpreting the results and implication of this form of therapy*

# SPACE FEVER

On **October 4, 1957**, the Soviet Union launched [Sputnik 1](#), the first artificial •  
satellite of Earth in the history of mankind.

On **November 3, 1957**, the Soviet Union launched the second •  
satellite, [Sputnik 2](#), and the first to carry a living animal, a dog  
named [Laika](#). [Sputnik 3](#) was launched on **May 15, 1958**, and carried a large  
array of instruments for geophysical research and provided data on  
pressure and composition of the upper atmosphere, concentration of  
charged particles, photons in cosmic rays, heavy nuclei in cosmic rays,  
magnetic and electrostatic fields, and meteoric particles.

After a series of failures with the program, the US succeeded with [Explorer](#) •  
[1](#), which became the first US satellite in space, on **February 1, 1958**. This  
carried scientific instrumentation and detected the theorized [Van Allen](#)  
[radiation belt](#)

# SPACE FEVER

On April 12, 1961, the USSR opened the era of manned spaceflight, •  
with the flight of the first *cosmonaut* (Russian name for space  
travelers), [Yuri Gagarin](#). Gagarin's flight, part of the  
Soviet [Vostok](#) space exploration program, took 108 minutes and  
consisted of a single [orbit](#) of the Earth.

On August 7, 1961, [Gherman Titov](#), another Soviet cosmonaut, •  
became the second man in orbit during his [Vostok 2](#) mission.

By June 16, 1962, the Union launched a total of six Vostok •  
cosmonauts, two pairs of them flying concurrently, and accumulating  
a total of 260 cosmonaut-orbits and just over sixteen cosmonaut-days  
in space

The first right heart catheterization in a human was performed by •  
Werner Forssmann on himself in 1929. Diagnostic cardiac  
catheterization was introduced by André Cournand and Dickinson  
Richards in the early 1940s, and selective coronary angiography was  
described by Mason Sones in the early 1960s. More recently, with the  
advent of catheter-based interventions, pioneered by Andreas  
Gruentzig in the late 1970s

# History of hypertension.

The modern **history** of **hypertension** begins with the • understanding of the cardiovascular system based on the work of physician William Harvey (1578–1657), who described the circulation of blood in his book "De motu cordis". ... This allowed blood pressure to be measured in the clinic

# WHEN WAS THE FIRST MEASUREMENT OF BP

Year **1733**. The first measurement of what was then called “the force of blood” is described in the book “Haema statics” in **1733**, by Stephan Hales. He used a water manometer to measure the blood pressure in the arteries of various animals

# WHO INVENTED THE BP

The sphygmomanometer was invented by **Samuel • Siegfried Karl Ritter von Baschin** **1881**. **Scipione Riva-Rocci** introduced a more easily used version in **1896**. In **1901**, pioneering neurosurgeon Dr. Harvey Cushing brought an example of Riva-Rocci's device to the USA, modernized it and popularized it within the medical community.

# WHEN WAS BP INVENTED

Riva-Rocci sphygmomanometer with cuff used by Korotkoff, who later discovered systolic and diastolic blood pressure. Modern blood pressure measurement was not developed until **1905**, when Dr. Nikolai Korotkoff discovered the difference between systolic blood pressure and diastolic blood pressure.



In 1958, the pharmacological properties of dichloroisoproterenol (**DCI**) were described, a  $\beta$ -antagonist discovered a few years before by the Eli Lilly group

DCI had no clinical utility but a replacement of the 3,4-dichloro substituents, with a carbon bridge to form a naphthylethanolamine derivative, **afforded a clinical candidate, pronethalol.**

**In April 1963, toxicity tests for pronethalol showed results of thymic tumours in mice.** Nevertheless, it was launched under the trade name Alderlin, as the first clinically useful  $\beta$ -blocker. The launch took place in November 1963 when many small-scale clinical trials had proved their effectiveness in angina and certain types of arrhythmias. **Pronethalol was only marketed for use in life-threatening situations.** Dr. James Black went on to create another  $\beta$ -blocker, called propranolol; **a non-selective  $\beta$ -blocker. Clinical trials started in the summer of 1964 and a year later, propranolol was launched under the trade name Inderal, only two and a half years after it had first been tested.<sup>[4]</sup> It turned out to have a higher potency than pronethalol, with fewer side effects**

# James W. Black

**Dr. James W. Black**, a **Scottish** pharmacologist whose discovery of beta blockers and another class of drugs extended the lives of millions of people with heart and stomach disorders and earned him a Nobel Prize in 1988, died on Sunday. He was 85. Mar 22, 2010

# Proportion of deaths attributable to leading risk factors worldwide (2000)

- High blood pressure •
- Tobacco •
- High cholesterol •
- Underweight •
- Unsafe sex •
- High BMI •
- Physical inactivity •
- Alcohol •
- Indoor smoke from solid fuels •

Atenolol, which was launched in 1976 under the trade name Tenormin. Atenolol is a selective  $\beta$ 1-receptor antagonist and was developed for the purpose of obtaining the “ideal  $\beta$ -blocker”. It soon became one of the best-selling heart drug

The first JNC report was published in 1977 and focused on treating elevated diastolic blood pressures, with the last official JNC report issued in 2003 as the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7).JNC 8 2014

The **Food and Drug Administration (FDA)** first approved lisinopril in 1987.

The drug company **Merck** developed lisinopril under the brand name Prinivil. In 2002, the **FDA** approved generic lisinopril.

The most common adverse effects of Captopril, [skin rash](#) and loss •  
of [taste](#),

[Enalaprilat](#) and [Lisinopril](#). These compounds both •  
have [phenylalanine](#) in R position which occupies the  $S_1$  groove in the  
enzyme. The result was thus these two new, potent tripeptide  
analogues with zinc-coordinating carboxyl group: Enalaprilat and  
Lisinopril

The first Randomized placebo-Controlled clinical Trial (RCT) in the • history of medicine was conducted by Medical Research Council (MRC of UK) in 1948 (studying the effectiveness of streptomycin for the treatment of tuberculosis). This provided the tool for scientific proof of efficacy of any treatment



Introduction of thiazide diuretics in late 50s made some headway in •  
successful treatment of hypertension and ambitious multicenter VA  
co-operative study (phase 1 and 2) started in 1964 for diastolic  
hypertension ranging between 90 and 129 mmHg and completed by  
1971 established for the first time that treating diastolic hypertension  
reduced CV events such as stroke and heart failure and improved  
mortality.

In the following decade, these results were confirmed for the wider •  
US and non-US population, including women and goal-oriented BP  
treatment to diastolic 90 became the standard therapy  
recommendation.

Isolated systolic hypertension (accounting for two- • thirds of the 70 million hypertensive population in USA alone) was not considered treatable until 1991 when SHEP study (systolic hypertension in elderly program) was completed and showed tremendous benefits of treating systolic BP over 160 mmHg using only a simple regimen using small dose chlorthalidone with addition of atenolol if needed.

In the next two decades, ALLHAT and other studies examined the • comparability of outcomes with use of different classes and combinations of antihypertensive drugs. Although diastolic BP goal was established as 90 in the late 70s and later confirmed by HOT(1998) study, the goal BP for systolic hypertension was not settled until very recently with completion of SPRINT study.

## Hypertension Optimal Treatment (HOT) 1998

First large randomized control trial to determine if lowering target diastolic blood pressure below 90 mmHg reduces CV events further

A The SPRINT study was somewhat similar to ACCORD study but was in non-diabetics and without any prior history of stroke. It enrolled about 9000 participants, many of them elderly and with stage 2–4 chronic kidney disease. The study was stopped in the first week of September 2015 per recommendation of the DSMB due to huge reduction in mortality (25%) and CV events (30%) in the group with systolic BP goal of 120.

Trials: 1967-70 VACoop, Veterans Affairs Co-operative studies; HDFP, hypertension • detection and follow-up trial (1979); MRFIT, multiple risk factor intervention trial (1982); MRC, Medical Research Council (UK)(1985); EWHPE, European Working Party High Blood pressure in the Elderly(1986); SHEP, systolic hypertension in the elderly program(1991); TOMHS, treatment of mild hypertension study (1993); DASH, dietary approaches to stop hypertension(1997); HOT, hypertension optimal treatment(1998); UKPDS, United Kingdom Prospective Diabetes Study (1998); AASK, African-American Study of Kidney Disease(2002); ALLHAT, antihypertensive and lipid lowering treatment to prevent heart attack trial(2002); ANBP, Australian National Blood Pressure Study(2003); ASCOT-BPLA, Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm(2005); CAFÉ, Conduit Artery Function Evaluation(2006); HYVET, hypertension in the very elderly trial(2008); ACCOMPLISH, avoiding cardiovascular events through combination therapy in patients living with systolic hypertension(2008); ACCORD, Action to Control Cardiovascular Risk in Diabetes(2010); SPRINT, systolic blood pressure intervention trial.stop in ist week 2015

**Resistant hypertension** is defined as blood pressure • that remains above goal despite concurrent use of three antihypertensive agents of different classes, one of which should be a diuretic. Patients whose blood pressure is controlled with four or more medications are considered to have **resistant hypertension**.



coronary dilators for the treatment of angina pectoris. This was •  
initiated by Janssen Pharmaceutica with diphenylmethyloperazines  
including lidoflazine, cinnarizine, flunarizine (Schaper et al., [1966](#)),  
and by Knoll AG with phenylalkylamines including verapamil, D600  
(Melville et al., [1964](#)). Bayer AG followed with dihydropyridines:  
nifedipine, nimodipine, nisoldipine (Vater et al., [1972](#)), and Tanabe  
with the benzothiazepine diltiazem (Sato et al., [1971](#)). Later Sandoz  
with isradipine (PN200-110) (Hof et al., [1984](#)), Pfizer with amlodipine  
(Burges et al., [1987](#)), and others followed with other dihydropyridines

The only groups who do not develop hypertension are certain isolated •  
tribes leading traditional hunter-gatherer existence. These groups do  
not experience age-related increase in BP and blood pressures ~  
young adolescents in Western communities.

Na<sup>+</sup> intake typically < 50mmol/day •

Common factor in all hypertension is decreased renal sodium •  
excretion 2 most important risk environmental risk factors for  
development of hypertension are BMI > 25 and sodium intake >  
100mmol daily

**thanks**