



# Platt versus Pickering: what molecular insight to primary hyperaldosteronism tells us about hypertension

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## DECLARATIONS

### Competing interests

MJB cites no current conflicts of interest but is seeking collaboration with companies developing aldosterone synthase inhibitors, in response to the Medical Research Council call for proposals in Stratified Medicine

### Funding

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### Ethical approval

All clinical studies received approval from one of the Cambridge Research Ethics Committees

### Guarantor

MJB

### Contributorship

MJA

## Summary

Recent genome-wide analyses have found 50 loci associated with variation in blood pressure but failed to advance understanding of the molecular basis of hypertension. Whether hypertension is not after all due to multiple common variants or is simply an order of magnitude more complex than previously suspected remains unsettled – in part because only a minority of subjects in the analyses had true hypertension. A better starting point than normotensive subjects for explaining hypertension may be the most common distinct cause of hypertension, primary hyperaldosteronism (PHA). The findings that 40% of patients with an aldosterone-producing adenoma (APA) of the adrenal have somatic gain-of-function mutations in a single gene, *KCNJ5*, and that this gene is, less frequently, mutated in inherited cases of PHA, potentially transform the understanding and management of hypertension. Firstly, they illustrate how hypertension could be due to a multiplicity of uncommon variants. Mutations that present with abnormal electrolytes and anatomy are the easiest to detect but are likely the tip of the iceberg. Secondly, we found a genotype:phenotype pattern, with *KCNJ5* mutations inducing larger APAs in the cortisol-secreting zona fasciculata in young women. Smaller APAs without *KCNJ5* mutations usually present in older men with resistant hypertension, having been overlooked earlier because of their size. This reflects their compact zona glomerulosa cells. Routine measurement of plasma renin in hypertension and a new positron emission tomography/computerized tomography allow prompt diagnosis and management of PHA before resistant hypertension ensues. Wider recognition of distinct phenotypes should permit earlier, specific treatment and reduce life-time risk of complications.

## Genetic analysis of complex disorders

The advent of genome-wide association studies (GWAS) has brought bitter-sweet results for complex disorders like hypertension. On the one hand, we can now finger – with the sort of statistical certainty previously reserved for forensic DNA

fingerprinting – dozens of sites in the genome that are contributing to inherited variation in blood pressure. On the other, the highest risk from any site is 1 mmHg of blood pressure – in most cases rather less; in no case can we be absolutely certain which specific gene is responsible, far less have any idea of where or how in the gene a variant is influencing blood pressure; and the

# Platt Versus Pickering An Episode In Recent Medical History

**Royal College of Physicians of London**



## **Platt Versus Pickering An Episode In Recent Medical History:**

, *Platt Versus Pickering* J. D. Swales, 1985 *National Library of Medicine Current Catalog* National Library of Medicine (U.S.), 1987 **Biomedicine in the Twentieth Century: Practices, Policies, and Politics** Caroline Hannaway, 2008-02-15 Biomedicine in the Twentieth Century Practices Policies and Politics is a testimony to the growing interest of scholars in the development of the biomedical sciences in the twentieth century and to the number of historians social scientists and health policy analysts now working on the subject The book is comprised of essays by noted historians and social scientists that offer insights on a range of subjects that should be a significant stimulus for further historical investigation It details the NIH s practices policies and politics on a variety of fronts including the development of the intramural program the National Institute of Mental Health and mental health policy the politics and funding of heart transplantation and the initial focus of the National Cancer Institute Comparisons can be made with the development of other American and British institutions involved in medical research such as the Rockefeller Institute and the Medical Research Council Discussions of the larger scientific and social context of United States federal support for research the role of lay institutions in federal funding of virus research the consequences of technology transfer and patenting the effects of vaccine and drug development and the environment of research discoveries all offer new insights and suggest questions for further exploration General Practice Under the National Health Service 1948-1997 Irvine Loudon, John Horder, Charles Webster, 1998 This is a history of general practice under the National Health Service covering the whole of the first 50 years from 1948 to the present *Hypertension: New Frontiers* HK Chopra, 2021-03-31 Hypertension is another name for high blood pressure It can lead to severe complications and increases the risk of heart disease stroke and death Blood pressure is the force exerted by the blood against the walls of the blood vessels Comprising more than 1000 pages this book is a complete guide to the diagnosis and management of hypertension Divided into 19 sections the text begins with an introduction to hypertension its causes risk factors and how it presents in different sectors of the population The next chapters discuss diagnostic methods and echocardiography The following sections cover hypertension associated with other disorders including heart failure stroke renovascular diseases metabolic syndrome and many more Numerous clinical management strategies are discussed in depth as well as cardio oncology nutrition and ECMO Extracorporeal Membrane Oxygenation a procedure that uses a machine to take over the work of the lungs and sometimes the heart A complete section is dedicated to paediatric cardiology and hypertension With an internationally recognised editor and author team the comprehensive text is highly illustrated with clinical photographs diagrams and tables The book also includes full online access Key points Comprehensive guide to diagnosis and management of hypertension comprising over 1000 pages Internationally recognised editor and author team Highly illustrated with clinical photographs diagrams and tables Includes full online access to the book **Current Catalog** National Library of Medicine (U.S.), First multi year cumulation covers

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**Hypertension as an Insulin-resistant Disorder** Ulf Smith,1991 It is generally agreed that primary hypertension is a multifactorial disorder where both genetic and environmemntal factors play an important role In recent years it has become evident that hypertension is closely associated with a number of metabolic risk factors for cardiovascular disease Insulin resistance and hyperinsulinemia seem to play a key role in the development of these risk factors An increasing body of evidence also suggests that insulin may be directly involved in the pathogenesis of hypertension Thus investigators representing different disciplines and approaches have critically reviewed the molecular and clinical evidence for the role of insulin in the pathogenesis of hypertension in this volume Also suggested are possible interactions of insulin with genetic and environmental factors This book succeeds in generating new approaches and defining areas needing further exploration as

well as contributing to the better understanding of the subject as a whole

### **Contemporary Directions in**

**Psychopathology** Theodore Millon, Robert F. Krueger, Erik Simonsen, 2010-02-25 This forward thinking volume grapples with critical questions surrounding the mechanisms underlying mental disorders and the systems used for classifying them Edited and written by leading international authorities many of whom are actively involved with the development of DSM V and ICD 11 the book integrates biological and psychosocial perspectives It provides balanced analyses of such issues as the role of social context and culture in psychopathology and the pros and cons of categorical versus dimensional approaches to diagnosis Cutting edge diagnostic instruments and research methods are reviewed Throughout contributors highlight the implications of current theoretical and empirical advances for understanding real world clinical problems and developing more effective treatments

### **Lithium and the Kidney** Sten Christensen, 1990

### **Frontiers of Diabetes Research** Kurt

George Matthew Mayer Alberti, R. S. Mazze, 1989 The selected theme for the above mentioned symposium was frontiers of research in non insulin dependent diabetes mellitus NIDDM The programme covered the molecular to the epidemiological included basic concepts as well as clinical applications and was contributed to by researchers from throughout the world The meeting was held in honour of Professors Harold Rifkin and Harry Keen both of whom have made significant contributions in wide areas of clinical diabetes research and practice The contents of this volume will serve as a state of the art synopsis of cutting edge research and clinical practice in NIDDM

### **Clinical Hypertension** James Ian Summers Robertson, 1992

Hardbound Recent years have seen remarkable advances in knowledge of the pathophysiology of hypertension and its treatment as a comparison of Volumes 1 and 2 with the present volume which is in part a revised account of many clinical aspects of hypertension first dealt with in these volumes will show The diagnosis and treatment of hypertension now permits the control of a wide range of vascular and cardiac disorders which comprise some of the most prevalent afflictions in the Western world Volume 15 of the Handbook of Hypertension series provides a detailed and accurate insight into the many disorders underlying high arterial pressure and its consequences Ten chapters of the book are devoted to primary or essential hypertension While detailed comprehension remains elusive we now possess early but distinct insights into both the genetic and environmental influences upon as well as the pathophysiology of this very prevalent affliction The remain

*Comprehensive Hypertension* Gregory Y. H. Lip, John Edward Hall, 2007 Here is today's most in depth reference for any cardiologist internist or nephrologist interested in hypertension Drawing from international experience in cardiology physiology and nephrology Drs Lip and Hall have assembled a group of section editors and contributors second to none You'll find the long term effects of primary and secondary hypertension and a lengthy section on hypertensions for special populations featured prominently Prevention and treatment of hypertension are covered in detail from lifestyle and diet issues to drug choice and delivery and the section on comparison of guidelines is unique to this book Find comprehensive coverage of hypertension including pathogenesis prevention and treatment all in one practical volume See the complete

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