Programme and Abstracts

XV Paavo Nurmi Symposium

Programming and Interventions on Risk Factors of Atherosclerosis In Childhood

13-15 December 2006 Oulu, Finland

Kansanterveyslaitoksen julkaisuja B 13/2006

Kansanterveyslaitos
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KTL-National Public Health Institute, Finland

Helsinki 2006

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Edita, Helsinki 2006

CONTENTS

FOREWORD

During the last few years it has been increasingly pointed out how the roots of atherosclerotic cardiovascular diseases go to childhood – and even to fetal issues. Research has also recently greatly advanced in the area of genetic susceptibility and the interaction between genes and environment.

Since the strong causal risk factors relate closely to certain behaviours and lifestyles, adoption of heart healthy lifestyles in childhood and youth is the ideal way of prevention and heart health promotion. This calls for both effective health education and health promotion as well as societal and policy measures to promote such developments in our societies.

The XV Paavo Nurmi symposium on "Programming and interventions on risk factors of atherosclerosis in childhood" is a three day symposium of highest scientific level to examine and discuss the latest knowledge on these issues – ranging from genetic predisposition to policy interventions. The symposium follows the previous successful Paavo Nurmi symposiums on other topics around cardiovascular diseases.

Paavo Nurmi Foundation was originally established by Paavo Nurmi, one of the greatest long distance runners of all times, to promote research to fight the epidemic of cardiovascular diseases. This XV Paavo Nurmi Symposium is arranged by the National Public Health Institute of Finland (KTL), with the financial support of Paavo Nurmi Foundation and with collaboration with several other partners.

This Paavo Nurmi Symposium will also highlight the establishment of a new KTL Department of Child and Youth Health in Oulu. This Department should help KTL to make a stronger contribution to national work on child and youth health in Finland, based on strong scientific base.

Oulu is the dynamic main city of Northern Finland. Visiting Oulu in December, before Christmas, means experience with a dark season with only a few hours of natural light. Thus it is a good time for spending the days inside in serious meetings. But it reminds also of the winter in the North, near Lapland, the country of Santa Claus.

On behalf of KTL and the organizers I want once more to thank everybody who has contributed to the preparations, the speakers and the participants, and not the least Paavo Nurmi Foundation.

Pekka Puska
Director General, KTL
Chair of the organizing committee of the XV Paavo Nurmi Symposium

XV Paavo Nurmi Symposium

Programming and interventions on risk factors of atherosclerosis in childhood

13-15 December 2006 in Oulu, Finland

OrganizingCommittee: Pekka Puska (Chair of the Organizing Committee), Juhani Eskola (Scientific Secretary), Erkki Vartiainen, Johan Eriksson, Leena Palotie, Marjo-Riitta Järvelin, Pekka Kare, Kimmo Kontula, Vesa Manninen, Olli Simell, Matti Uhari, Eeva-Liisa Urjanheimo, Eeva Kuuskoski

SCIENTIFIC PROGRAMME

Wednesday, 13 December 2006:

Opening of the symposium

12.30 - 13.00 Pekka Puska (Chairman of the Organizing Committee)

13.00 - 13.15 Maria Kaisa Aula (Ombudsman for Children in Finland)

13.15 – 13.30 Film of Paavo Nurmi

Afternoon session 1: **Genetic predisposition /** Chair: Juhani Eskola

13.30 – 14.00 Leena Peltonen, Helsinki, Finland: Special population resources in gene hunt of cardiovascular diseases

14.00 – 14.30 Thomas J. Hudson, Montreal, Canada: Genome wide analyses and genetic profiles for cardiovascular traits

14.30 – 15.00 Philippe Froguel, London, UK: Genetics behind cardiovascular diseases and metabolic syndrome

15.00 – 15.30 Mark McCarthy, Oxford, UK: Genes behind type 2 diabetes and obesity

Coffee break

Afternoon session 2: **Developmental origins of adult disease /** Chair: Juhani Eskola

16.00 – 16.30 David Barker, Southampton, UK: The origins of the "fetal origins" hypothesis: How it all started.

16.30 – 17.00 Johan Eriksson, Helsinki, Finland: Fetal and early growth and adult health outcomes – lessons from the Helsinki Birth Cohort Studies

17.00 – 17.30 Peter Gluckman, Auckland, New Zealand: Taking the developmental origins of adult disease hypothesis further

Dinner

Thursday, 14 December 2006:

Morning session 3: **Early pathogenesis of atherosclerosis /** Chair: Johan Eriksson

09.00 – 09.30 Nils H Sternby, Lund, Sweden: Pathobiological determinants of atherosclerosis in youth

09.30 – 10.00 Petri Kovanen, Helsinki, Finland: Molecular pathogenesis of hypercholesterolemia

Coffee break

Morning session 4: **Programming of cardiac diseases in childhood and adolescence /** Chair: Johan Eriksson

10.30 – 11.00 Trudy Burns, Iowa City, USA: Long-term prognostic significance of childhood blood pressure levels: The Muscatine Study

11.00 – 11.30 Ricardo Uauy, Chile: Nutrition, child growth and chronic disease prevention

11.30 – 12.00 Marjo-Riitta Järvelin, Oulu, Finland: Risk factors of cardiovascular traits identified in birth cohorts

Lunch

Thursday, 14 December 2006:

Afternoon session 5: **Intervention on risk factors in childhood /** Chair: Marjo-Riitta Järvelin

13.00 – 13.30 Matti Uhari, Oulu, Finland: Blood pressure in children as a risk factor for cardiovascular diseases

13.30 – 14.00 William Dietz, Atlanta, USA: Weight control in children

14.00 – 14.30 Gerald Berenson, New Orleans, USA: Lessons from BOGALUSA project

14.30 – 15.00 Jorma Viikari, Turku, Finland: Lessons from the Cardiovascular Risk in Young Finns and the STRIP studies

Coffee break

Afternoon session 6: **Behavioural interventions /** Chair: Marjo-Riitta Järvelin

15.30 – 16.00 C. Anderson Johnson, Los Angeles, USA: Theory and practice of promoting healthful lifestyles in response to environmental and intrapersonal challenges

16.00 – 16.30 Shrinath Reddy, New Delhi, India: Prevention of cardiovascular risk factors in developing countries

16.30 – 17.00 Hein de Vries, Maastricht University, Hollanti: New developments in smoking prevention

17.00 – 17.30 Erkki Vartiainen, Helsinki, Finland: Effect of school interventions on smoking in young children

Dinner

Friday, 15 December 2006:

Morning session 7: **Preventive programs and policies /** Chair: Erkki Vartiainen

09.00 – 09.30 Li Villard, Stockholm, Sweden: Policies in adolescent cardiovascular health promotion

09.30 – 10.00 Brian Oldenburg, Queensland, Australia: Promoting health and preventing disease across the life-course: issues and challenges

10.00 – 10.30 Darwin Labarthe, Atlanta, USA: US strategy for cardiovascular disease prevention

Coffee break

Morning session 8: **Preventive programmes and policies (cont.) /** Chair: Erkki Vartiainen

11.00 – 11.30 Imogen Sharp, London, UK: Policy environment for children's healthy growth

11.30 – 12.00 Ximena Berrios, Chile: School based policies to prevent chronic disease risk factors in Chile

12.00 – 12.30 Pekka Puska, Helsinki, Finland: National and international policies to promote heart health in youth

Lunch

INTRODUCING THE SPEAKERS

Maria Kaisa Aula, 44, is Finland's first Ombudsman for Children and holds a Licenciate of Political Sciences. Earlier, she was a Member of Parliament and a special assistant to the prime minister. From 2004-2005 she chaired the Central Union for Child Welfare in Finland. Her term as Ombudsman began 1 September 2005.

The Ombudsman monitors the living conditions of children and young people, and influences social development policy by strengthening the viewpoint of children. The duties of the Ombudsman also include reinforcing the participation of children and young people and conveying their opinions in decision making processes.

David Barker MD,PhD,FRS is a physician. He is Professor of Clinical Epidemiology at the University of Southampton, UK, and Professor in Medicine at Oregon Health and Science University, Portland, US. He was formerly Director of the Medical Research Council Epidemiology Unit at Southampton. His research has shown that low birthweight is associated with an increased risk of cardiovascular disease and type 2 diabetes in later life.This has led to the hypothesis that chronic adult disease originates through the persisting effects of the maternal and early postnatal environment on the developing organs and systems of the body.

Gerald Berenson, Professor of Medicine (Cardiology) Pediatrics and Epidemiology – Interested in cardiovascular diseases and prevention – Principal Investigator of the Bogalusa Heart Study over the past 34 years, supported by NHLBI and NIA of the National Institute of Health.

Trudy Burns, MPH in biostatistics and Ph.D. in biostatistics and epidemiology from the University of Michigan. On the faculty at the University of Iowa since 1982. Currently Professor in the Department of Epidemiology, College of Public Health; the Department of Pediatrics, Carver College of Medicine; and the Parent Child Family Area of Study, College of Nursing. Investigator with The Muscatine Study since 1983

William H. Dietz, M.D., Ph.D. Dr. Dietz is the Director of the Division of Nutrition and Physical Activity at the CDC. Prior to his appointment to the CDC, he was a Professor of Pediatrics at the Tuft's University School of Medicine, and Director of Clinical Nutrition at the Floating Hospital of New England Medical Center Hospitals. He received his MD from the University of Pennsylvania in 1970 and a Ph.D. in Nutritional Biochemistry from MIT. He is a member of the Institute of Medicine and a recipient of the Holroyd-Sherry award from the AAP for his contributions to the field of children and the media.

Johan G. Eriksson, Dr., Graduated from University of Helsinki (1986). Specialised in internal medicine at Helsinki University Central Hospital (1994) and in General Practise (2005). Head of Diabetes Unit at National Public Health Institute (2000-6). Professor in General Practise, University of Helsinki (2006-). Over 150 peer-reviewed original articles primarily within the field of diabetes and developmental origins of health and disease. PI of the Helsinki Birth Cohort Study investigating the early programming of adult disease.

Juhani Eskola, M.D., Ph.D. has worked after graduation as a clinician (first as a general practitioner, later as paediatrician and paediatric infectious disease specialist) in Helsinki, Finland. From 1991 through 1999 he served at KTL as Research Professor and Head of Department of Vaccines. During 1997-1998 he was Visiting Professor at Imperial College in London, and in 2000-2003 Senior Vice President of Aventis Pasteur in Lyon, France, where his responsibilities included clinical development of new vaccines as well as global medical affairs. Currently Juhani Eskola is Professor and Deputy Director General of KTL. His main responsibilities are in the area of strategic planning and support of research in the Institute.

Philippe Froguel, MD, PhD is 48 years old. He is married, has 3 daughters and lives in London, UK. He passed his Medical Degree in 1986 (Paris 6 University, St Antoine Medical School), and he obtained a PhD in 1991 (Paris 7 University). At this time he was head of the diabetes laboratory at CEPH (Human Polymorphism Study Centre, Paris, headed by Pr Jean Dausset, Nobel prize winner). He served as CEPH Secretary general and was member of the board of the French Genethon genomic centre. In 1995, he accepted a position of Head of Human Genetics at the CNRS Institute of Biology, Pasteur Institute, Lille, France. In 2000, he was appointed Professor of Molecular Genetics and Experimental Diabetes at Queen Mary College and he established the Barts and The London Genome Centre. He moved in 2003 to Imperial College as Professor of Genomic Medicine, and currently head of Section of Medical Genetics and chair of the Imperial College Genome centre located at Hammersmith hospital (which comprises high throughput DNA genotyping and sequencing, microarrays and proteomics). In UK, Philippe Froguel is PI of a MRC program grant on "polygenic obesity" and co-PI of the new NHS Diabetes clinical network.
His scientific carrier is entirely focused on the genetics of complex traits in human, especially in diabetes (most referred world wide scientific author 1991-2001 in the diabetes field http://www.esi-topics.com/diabetes/authors/b1a.html) and in obesity and on their vascular complications. He published about 250 publications so far. He has developed original candidate gene, positional cloning and positional candidate gene approaches in the "diabesity" field which have lead to major discoveries. For this purpose, he has established one of the largest collection of diabetic and obese families (DNA, cell lines, and phenotypic data), including 2,400 multiplex families, and case and control cohorts from different ethnic groups (altogether >25,000 samples).
Philippe Froguel identified some of the first genes responsible for monogenic T2D and obesity: glucokinase, the first type 2 diabetes gene, -Froguel, nature, 1992, Vionnet, nature, 1992, Froguel, NEJM, 1993), HNF-1 (Vaxillaire, nature genetics, 1995, nature, 1996), leptin receptor (Clément, nature, 1998), MC4R (Vaisse, Nature genetics, 1998, Vaisse, JCI, 2000), IB1/JIP (Waeber, nature genetics, 2000). Several candidate genes for diabetes and obesity and CHD were identified by his group: beta 3-adrenergic

receptor (Clément, NEJM, 1995), Paraoxonase (Ruiz, Lancet, 1995), glucagons receptor (Hager, nature genetics, 1996), potassium channel KIR 6.2 (Hani, Diabetologia, 1997). He has completed several genome scans in diabetes (Vionnet, AJHG, 2000, Mori, Diabetes 2002, Martin, Diabetes, 2002, Frayling, Diabetes, 2003), and he published in 1998 the first genome scan of obese families obesity (Hager, nature genetics, 1998) which lead in 2003 to the identification of a massive obesity susceptibility gene, GAD2 on chromosome 10p. The T2D French and Japanese GS as well as the CHD Mauritian Genome Scan (Franck, HMG, 2001) lead to the identification of a strongly linked chromosomal region on 3q27. Subsequently, Froguel's major contribution was to recognize the adipocyte-secreted ACRP30/adiponectin, encoded by the chromosome 3q27 APM1 gene, as an important marker of the risk for insulin resistance and T2D in both human and animal models (Yamauchi, nature genetics 2001 and 2002, Vasseur, HMG, 2002, Hara, diabetes, 2002, Populaire, Diabetologia 2003, Gibson, Diabetes 2004, Vasseur Diabetologia 2005). A major common focus of the 2 groups (in Lille and in London) is severe obesity in children, a major world wide concern strongly associated with early onset diabetes. A full genome scan showed major regions of linkage with obesity, including one on 6q where recently evidence for a contribution of variants of the insulin inhibitor ENPP1/PC1 gene in diabesity was found (Meyre, nature genetics, 2005). Another recent achievement is the discovery of the TGF-beta induced gene KLF11/TIEG2, a transcription factor responsible for both monogenic and polygenic T2D and for pancreatic cancer (Neve, PNAS, 2005). A comprehensive review of the human genetics of obesity state of the art was published in 2005 (Bell C, nature reviews genetics, 2005).

PD Gluckman, Professor, FRS, University Distinguished Professor, Professor of Paediatric and Perinatal Biology, Director, Liggins Institute, Director, National Research Centre for Growth and Development, University of Auckland.

Dr. **Tom Hudson** is President and Scientific Director of the Ontario Institute for Cancer Researchm and Interim Director of the McGill University and Genome Quebec Innovation Centre. Dr. Hudson is internationally renowned for his work in Genomics. At the Whitehead Institute, Dr. Hudson led the effort to generate dense physical and gene maps of the human and mouse genomes. Hudson and his team at McGill University were founding members of the International Haplotype Map Consortium. Dr. Hudson's interests in human genetic diseases focus on the dissection of complex genetic diseases. Dr. Hudson is co-founder and Chief Scientific Officer of P3G, an international consortium in population genomics. Dr. Hudson is editor-in-chief of the journal Human Genetics.

C. Anderson (Andy) Johnson is the director of the Institute for Health Promotion & Disease Prevention Research (IPR), and Sidney Garfield Professor of Health Sciences and Professor of Preventive Medicine & Psychology at the University of Southern California. He is married to Charisse Vega, a designer. Children include a son, Dylan, and a daughter, Caroline. Johnson earned his BA in psychology and PhD in social psychology with a minor emphasis in neuroscience from Duke University. Prior to USC he did postdoctoral work in environmental psychology at the National Bureau of Standards and held a faculty position at the University of Minnesota. His research contributions include

mechanisms of action in community based approaches to tobacco, alcohol, and drug abuse prevention. His recent research has focused on social and cultural change acting in combination with genetically and environmentally driven dispositional characteristics to influence health risk behaviors, including socio-cultural and dispositional interactions influencing the effectiveness of smoking and alcohol abuse prevention programs. Johnson is director of the Pacific Rim Transdisciplinary Tobacco & Alcohol Use Research Center and co-director of the USC Transdisciplinary Drug Abuse Prevention Research Center. He is the founding director of the China Seven Cities Study, a longitudinal study of tobacco use and lifestyles in seven of China's largest cities.

Marjo-Riitta Jarvelin, MD, PhD, Pediatrician, is Professor in Lifecourse Epidemiology at Imperial College London, University of London, UK, and Professor in Public Health in the Department of Public Health Science and General Practice at the University of Oulu, Finland. She holds MSc in environmental epidemiology and policy from the University of London, a Ph.D. in Medical Science from the University of Oulu, Finland, and is a faculty member of Public Health Medicine, the Royal Colleges of Physicians of the United Kingdom. Prof. Jarvelin is a divisional director of postgraduate studies at Imperial. She has been running large-scale population based studies since 1983 and is the director of the Northern Finland Birth Cohort Study (1995-) started 1960s to explore the association between early life factors and later disease risk. Her team is currently working on the genetic and environmental origins of multifactorial diseases in close collaboration with the other research groups from the UK, Finland, Denmark, Sweden, Greece and the USA; funded e.g. from The EU, Wellcome Trust, MRC, NIH, the Academy of Finland and The Nordic Council of Ministers.

Petri T Kovanen, M.D., Ph.D., Dr. Kovanen has received his medical degree 1970 at the University of Basle, Switzerland, and then his Ph.D degree at the University of Helsinki, Finland. He conducted his postdoctoral work (1976 – 1980) at the University of Texas, Health Science Center at Dallas, Department of Medicine and Department of Molecular Genetics. After his return to Finland, he completed his residency in internal medicine at the University of Helsinki. In 1984 he was appointed as Scientific Director of Wihuri Research Institute, Helsinki, and currently serves as Director of the Institute. His main research interests focus on the pathogenesis of atherosclerosis, both early atherogenesis with emphasis on the mechanisms of lipid accumulation in the arterial wall, and late atherogenesis with emphasis on the generation of vulnerable plaques. The objective of his investigations is to better understand the chain of molecular events in the arterial wall starting in the modification of the accumulated lipids, then leading to local inflammation, and ultimately, to clinical complications such as myocardial infarction and stroke.

Darwin R. Labarthe (MD, MPH, PhD)is currently Director, Division for Heart Disease and Stroke Prevention, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention (CDC), Atlanta, USA

Mark McCarthy is Robert Turner Professor of Diabetes at the University of Oxford, UK, based in the Oxford Centre for Diabetes, Endocrinology & Metabolism (OCDEM) and the Wellcome Trust Centre for Human Genetics. He qualified in medicine at

Cambridge and undertook subsequent training (in diabetes and endocrinology) at the London Hospital. His research focus on the genetics of type 2 diabetes was fostered during time with Dr Eric Lander and colleagues at the Whitehead Institute in Cambridge, MA. Following return to the UK he was appointed as Professor of Genomic Medicine at Imperial College, London, before his move to Oxford in 2002. Together with colleagues in the UK and Europe, Prof McCarthy has pioneered collection and use of large sample cohorts for linkage and association studies in type 2 diabetes. These approaches are starting to bear fruit with increasing success in identifying replicated regions of linkage and in characterisation of susceptibility variants. Currently, Prof McCarthy is involved in several large projects that make use of recent advances in genotyping technology (including the international 1q consortium and the Wellcome Trust Case Control Consortium) and in the understanding of patterns of human linkage disequilibrium to map T2D susceptibility genes. A related interest is to develop insights into the early events in the pathogenesis of diabetes through the identification of early transcriptional, proteomic and metabonomic biomarkers of metabolic decompensation. The aim of this work is to develop tools that can be used to improve prediction, prevention and management of diabetes and related conditions.

Brian Oldenburg is Professor and Chair of International Public Health at Monash University, Melbourne, Australia. His research over more than 25 years spans the social/behavioural sciences and public health, with the major focus having been on the primary and secondary prevention and management of chronic disease, particularly heart disease and diabetes. This has included intervention trials, conducted in health care settings, work organisations, schools and other community settings in Australia and internationally, including most recently, China and Finland. A more recent and major research focus has been on chronic disease, socioeconomic health inequalities, social disadvantage and interventions with Australia's indigenous people. He also has a broader interest in translational and policy-relevant research in Australia and internationally.

Leena Peltonen is Academy Professor in the University of Helsinki and National Public Health Institute in Biomedicum Helsinki, Finland and a visiting professor at Broad Institute in Boston. She is a director of the Center of Excellence in Common Disease Genetics. With over 400 publications, Dr. Peltonen is among leading molecular geneticists world-wide. She has received several science prizes and was recently elected as a Foreign Associate Member of the National Academies USA, Institute of Medicine (IOM).

Pekka Puska, (M.D., Ph.D., M.Soc.Sc.)Professor, has served as the Director General of the National Public Health Institute (KTL) since late 2003. Professor Puska's career at KTL began already in 1978 with the position of Director for the Department of Epidemiology and Chronic Disease Prevention. During this time he led the internationally known North Karelia Project, a successful population-based prevention of non-communicable diseases. Prior to his present position he served as the Director for Non-communicable Disease (NCD) Prevention and Health Promotion at the WHO Headquarters in 2001–2003.

Matti Uhari, MD, MSc (epidemiology),Professor of Pediatrics, Department of Pediatrics University of Oulu. Associate Professor of Pediatrics since 1984, Professor of

Pediatrics since 1998. Master of Science in Epidemiology 1983 (London School of Hygiene and Tropical Medicine).
Ricardo Uauy M.D. Ph.D. Medical Doctor University of Chile 1972, Pediatrics at Harvard and Neonatology at Yale. PhD Nutritional Biochemistry from M.I.T. 1977. Professor of Nutrition at INTA University of Chile (1985) and Professor of Public Health Nutrition at the London School of Hygiene and Tropical Medicine University of London (2002). Member of the Chilean Academy of Medicine (2002). Received the McCollum award of the American Society for Nutritional Sciences (USA) 2000. PAHO/WHO 2005 Abraham Horwitz award for Leadership in Inter-American Health. He is president of the IUNS International Union of Nutritional Sciences 2005-09.

Erkki Vartiainen, MD, and Ph.D. in Public health. He is professor and director of Department of Health Promotion and Chronic Disease Prevention in National Public Health Institute in Finland. His main research interest has been cardiovascular disease prevention in adults and children. He has been mainly working on community and school based health promotion and disease prevention programmes. He has 325 publications in scientific journals. He has been working as a Consult for World Bank, WHO and EU in cardiovascular and other chronic diseases prevention and health promotion in several developed and developing countries.

Li Villard is a physiotherapist and a PhD in cardiovascular prevention at the Karolinska Institutet, Stockholm, Sweden. She is currently continuing her research at the Department of Medicine, Unit of Cardiology, Karolinska Institutet as well as working clinically at the National Childhood Obesity Centre, Karolinska University Hospital where she treats obese children and adolescents and coaches them to be more physically active.

Jorma Viikari is Professor (chair) of internal medicine, University of Turku, Turku, Finland (2002-). He has been Coordinator of the Cardiovascular Risk of Young Finns Study since 1978 and Coordinator of the STRIP-baby project (Special Turku coronary Risk factor Intervention project for babies) since 1990.

Hein de Vries, Ph.D., Professor in Cancer Prevention and Health Promotion, Department of Health Education and Health Promotion, Maastricht University, Endowed chair for the Dutch Cancer Society on Cancer Prevention and Health Promotion**,** Honorary Research Consultant on Cancer Prevention to the Medical Research Council of South Africa, Catharina Pijls Award for the dissertation "Smoking prevention in Dutch adolescents", November 29, 1990. Research agreement between the department of Health Education and the Dutch Smoking and Health Foundation, Co-founder (with Prof. Dr. Anne Charlton) of ENYPAT, Steering group member and member of Adivisory Board of the European Network for Young People Against Tobacco (ENYPAT), Brug, H. & De Vries, H. (1999). Special Issue Computer Tailored Education; Guest Editors for Patient Education and Counseling, Research Collaboration with Nelson Mandela School of Public Health**,** Department of Community Health**,** Durban, South Africa, Visiting professor Cancer Prevention Research Center, University of Rhode Island, RI,US

ABSTRACTS

Special population resources in gene hunt of cardiovascular diseases

Leena Peltonen, M.D., Ph.D., Academy Professor, National Public Health Institute and University of Helsinki, Finland; The Broad Institute, MIT, Boston, MA, USA

The Human Genome Project produced a high number of catalogued sequence variants enabling genome-wide studies of genetic loci behind common disease-related phenotypes. European population isolates like Finland have been very useful for identification of disease genes; in such isolates genetic drift leads to an overabundance of disease-alleles for particular disorders, and a high proportion of patients potentially share these alleles, identical by descent. The founder effect, drift and isolation facilitate efficient use of linkage disequilibrium and this emphasize the value of detailed information of the population history as the crucial factor in genetic studies of common diseases.

I will describe the features of the Finnish population and our efforts to search for disease genes for rare and common phenotypes. Our studies on lactose intolerance, cardiovascular diseases and neuropsychiatric traits exemplify the strategies used to identify disease genes in various Finnish data sets and study samples. I will also describe our recent efforts on the EU-funded European-wide twin study, Genomeutwin (www.genomeutwin.org) Our data demonstrate how the impact of specific allelic variants of disease genes, identified in families, can be addressed in large population cohorts containing excessive amount of quantitive phenotype information.

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Boomsma, D., Busjahn, A., Peltonen, L. The classical twin studies and beyond. Nature Review Genetics 3: 872-883, 2002.

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K. Komulainen, M. Alanne, K. Auro, R. Kilpikari, P. Pajukanta, J. Saarela, P. Ellonen, K. Salminen, S. Kulathinal, K. Kuulasmaa, K. Silander, V. Salomaa, M. Perola, L. Peltonen: Risk alleles of USF1 gene predict cardiovascular disease of women in two prospective studies. PloS Gen 2(5); e69, 200

Genetic analysis of 100 loci for coronary artery disease and associated phenotypes

Thomas J. Hudson, Guillaume Paré, David Serre, Alexandre Montpetit, James C. Engert, Diane Brisson, Daniel Gaudet, Sonia Anand and Salim Yusuf
McGill University, Chicoutimi Hospital, and McMaster University, Canada

Recent studies of genetic variation across the human genome has led to concepts for a systematic approach to study a large fraction of human genes, using strategies that exploit linkage disequilibrium (ie, correlations between nearby markers). To exploit these strategies, the International HapMap Consortium generated a haplotype map of the human genome to enable the human genetics community to efficiently screen for genes predisposing to complex traits. In my talk, I will present a brief overview of the HapMap project, followed by applications in mapping genes for coronary artery disease (CAD).
I will first describe a project involving the analysis of 884 individuals from 142 families (with average sibships of 5.7) as well as 558 cases and controls from the Saguenay Lac St-Jean region of north-eastern Quebec using 1536 single nucleotide polymorphisms (SNPs) in 103 candidate genes for CAD. I will also describe progress in analyzing the same gene set in the INTERHEART case-control study that involved about 29,000 people from 52 countries involving all major ethnic groups, for both sexes and all ages. We have initially targeted three major population samples included in INTERHEART, with ancestries from Northern Europe, South Asia and the Middle-East, which involve over 10,000 participants. Issues of study design when using multi-ethnic samples, and methods to evaluate population stratification within and across population samples have been critical steps in this project.

Genes behind type 2 diabetes

Mark McCarthy, Robert Turner Professor of Diabetes, Oxford Centre for Diabetes, Endocrinology and Metabolism (OCDEM), Oxford, UK

The substantial inherited component of type 2 diabetes (T2D) susceptibility means that important insights into disease pathogenesis can be obtained by susceptibility gene identification and characterisation. Whilst there has been spectacular success in identifying genes responsible for monogenic forms of diabetes, characterisation of genes influencing "typical" multifactorial T2D has proceeded more slowly: each individual susceptibility variant has only a modest effect on disease risk. Until recently, much of the effort to define such variants has been compromised by methodological limitations, of which inadequate sample size has been most important. Many existing claims of variants associated with T2D are probably spurious.

These difficulties are increasingly surmountable. Several T2D-susceptibility genes have been identified through candidate gene and positional cloning approaches. For example, common variants in PPARG and KCNJ11 each predispose to T2D with odds ratios of ~1.2 across many studies in diverse populations. The consequences of variation within TCF7L2 on T2D risk seem even greater. These examples emphasise the improving prospects for T2D gene identification. It is clear that: (a) large studies are required for robust identification of susceptibility variants; (b) examination of genes of interest needs to be exhaustive because unheralded functional variation may occur well outside coding regions; and (c) diabetogenes so far identified emphasise the relative importance of inherited effects on beta-cell function, rather than insulin action.

A comprehensive view of the landscape of genetic susceptibility to T2D is within sight. By typing sufficient markers (many hundreds of thousands) in large enough sample sets (many thousands) we can expect (under realistic assumptions) to capture a high proportion of the variants with meaningful disease associations. A number of such genomewide association studies are underway, including our own involvement in the Wellcome Trust Case Control Consortium. These studies present very significant informatics and analytical challenges and will require novel high-throughput approaches to relate genetic association findings to relevant sources of functional and biological data. However, we can expect them to provide a wealth of insights into the inherited basis for T2D susceptibility.

The origins of the 'fetal origins' hypothesis

D J P Barker, MD,PhD,FRS, Professor of Clinical Epidemiology at the University of Southampton, UK, and Professor in Medicine at Oregon Health and Science University, Portland, US.

The 'fetal origins' hypothesis was first put forward in an attempt to explain the paradox that while coronary heart disease increases with rising prosperity, it is more common in poorer areas of western countries and among poorer peoples. For the disease to occur two influences seem to be necessary: one associated with affluence for which the high energy western diet is the obvious candidate; and the other associated with poverty. Ecological data suggest that the influences linked to poverty either act through the mother or through living conditions in early postnatal life. Longitudinal studies have now provided clear evidence of this.

Fetal and early growth and adult health outcomes – lessons from the Helsinki Birth Cohort Studies

Johan G. Eriksson, National Public Health Institute and University of Helsinki

Experiences during critical periods of early development may through the mechanisms of programming have long-term consequences on later health outcomes. Observations linking a small body size at birth with several adult health outcomes have greatly added to our understanding of the early origins of disorders like coronary heart disease, hypertension and type 2 diabetes.
Two study cohorts consisting of 15846 individuals born at Helsinki University Central Hospital and who grew up in Helsinki have been followed.
The growth patterns predisposing to coronary heart disease is characterized by a small body size at birth and thinness through infancy, followed by accelerated gain in weight and body mass index later in childhood. The early growth patterns predisposing to type 2 diabetes in adulthood very much resemble the growth patterns of CHD.
There are several possible mechanisms through which a non-optimal early growth associated with accelerated weight gain in childhood could predispose to these diseases. These mechanisms include changes in organ size and function, programming of hormonal settings and growth factors as well as programming of gene expression. Most data suggest that the development of many non-communicable diseases involve a number of interactions including genetic ones.
To get a better understanding of the patterns of growth affecting adult health outcomes a life course approach to the development of chronic diseases needs to be taken.

Taking the Developmental Origins of Health and Adult Disease Paradigm (DOHAD) further

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Since the original epidemiological finding of an association between birth size and later disease risk, there has been much confirmation and there can be no doubt that there are relationships between environmental influences in early life and alterations in later disease risk. Indeed the scope of diseases in which "programming has been implicated has grown. Experimental data have shown that a variety of developmental cues can induce changes in physiology/structure that could explain the epidemiology. Emerging knowledge in developmental plasticity, developmental biology and epigenetics provides possible mechanistic bases. From these there has been considerable development of conceptual explanations for the DOHAD paradigm. However, the relative importance of the phenomenon for the ecology of human disease in different populations remains uncertain and the implications for prevention and intervention remain uncertain and unproven. There are many outstanding questions which will inform the future basic and clinical research. These include: *Underlying processes:* Within the scope of DOHAD, what is developmental plasticity and what is developmental disruption and to what extent are these separate? Does developmental toxic exposure exploit the mechanisms of developmental plasticity? Is human disease a maladaptive consequence of an evolutionarily protected process? To what extent is "programming" an integrated response involving life history tradeoffs rather than a series of single cue/response relationships? What is the significance of gender differences? To what extent do epigenetic phenomena underpin environmentally induced changes in developmental plasticity and programming? To what extent does non-genomic inheritance play a role in the etiology of human disease and developmentally induced disease risk?

The burden of disease: How important are early environmental factors in the ecology of human disease? What is the contribution of preconceptual, periconceptual, embryonic, fetal, neonatal, infant and childhood environmental factors in adding to disease risk in *current* populations? How can this be determined? To what extent do demographic change and the nutritional transition influence the changing pattern of developmentally induced disease, what is the role of maternal constraint? How does developmental induction by nutritionally poor cues relate to induction by nutritionally excessive cues or are these different processes. To what extent do polymorphisms interact with developmental cues in determining added or lesser disease risk and to what extent are these population specific?

Postnatal amplification: How do early life exposures alter the response of the organism to later life exposures? What is the role of catch-up growth? Does the degree of developmental mismatch determine the degree of added disease risk?

Implications for prevention and intervention; How do we define programming prospectively in a human population – can the effects of programming be predicted? To what extent and over what periods of development is programming reversible, either generally or in a specific organ, by what mechanisms and how can this be defined and monitored? How does this knowledge inform individual and population health interventions in the developed and developing worlds? What interventions are logical and ethical and how can these be tested.

WHO/ISFC study of pathobiological determinants of atherosclerosis in youth (PBDAY study)

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The study was a ten-year multinational collaborative study performed 1986 to 1996 and supported by the World Health Organization, the International Society and Federation of Cardiology and various grants to the participating laboratories. The final report, which forms the basis for this presentation, was prepared by Dr P. Nordet, Geneva, professor J.E.Fernandez-Britto, Havana and prof N.H.Sternby, Malmo.

The study included subjects aged 5-34 years, of both sexes, and from 11 centres in 11 countries including both developed and developing countries from five WHO regions. These centres were selected from a pilot study in 18 centres in 15 countries. From each centre we collected background epidemiological information and from each case general information, arterial specimens (aorta and coronary arteries), kidney and myocardial tissue. In some centres also liver tissue and adipose tissue was collected.

The analyses were performed in seven reference centres with different morphometry methods, and with biochemical, histochemical, immunohistochemical and ultrastructural techniques.

Data was processed from 1277 cases, 958 males and 319 females. In age group 5-14 we had 133 cases, in ages 15-24 was had 509 and in ages 25-34 we had 635 cases.

Atherosclerosis, in the form of fatty streak, develop in all individuals early in life, independent of sex or geographical origin, their greatest development between 15 and 25 years of age. Fibrous plaques begin developing slowly during the second decade of life, progress steadily the third and more rapidly during the fourth. Complicated and/or calcified plaques are very rare below 30 years of age, they begin to appear regularly in the fourth decade of life. The prevalence and extent of raised lesions (all types except fatty streaks) is higher in countries with a high prevalence of risk factors and high mortality rates for cardiovascular diseases, e.g., Cuba, Germany, Hungary and Lithuania. Well known risk factors (hypertension, diabetes and smoking) were shown to have a great influence on the development of atherosclerosis and also on intimal thickness and intimal cellular density.

Other detailed findings will be discussed.

The overall findings reiterate the need for promotion of a healthy lifestyle early childhood.

Molecular pathogenesis of hypercholesterolemia

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Atherosclerosis is the leading cause of death worldwide. Insudation of atherogenic lipoproteins, notably of low density liporoteins (LDL), into the artery wall is integral to atherogenesis. The atherosclerotic disease process has its origins in childhood, and even in the fetal period, if the level of LDL is severely elevated. Much research over the past quarter century has
adressed the genetic causes of primary hypercholesterolemia. In the population at large, the level of LDL results from the complex interactions of small effects of numerous genetic loci. However, 5 specific monogenic disorders are known to increase the level of LDL. These (and the respective defective genes) are familial hypercholesterolemia (LDL receptor gene); familial ligand-defective apoB-100 (apoB gene); autosomal recessive hypercholesterolemia (ARH gene); sitosterolemia (ABCG5 or ABCG8 gene), and cholesterol 7-alpha hydroxylase deficiency (CYP7A1 gene). It is hoped that molecular dissection of the pathogenesis of these rare diseases will aid our understanding of the more common causes of hypercholesterolemia, and so pave the way to new therapeutic venues in the combat against atherosclerotic cardiovascular diseases.

Long-term prognostic significance of childhood blood pressure levels: The Muscatine Study

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Hypertension is detectable in children and adolescents and its prevalence is increasing, due in large part to the increasing prevalence of obesity. The Muscatine Study adult cohort has been followed for more than 35 years; blood pressure and body size measurements are available at several time points. The long-term prognostic significance of childhood blood pressure levels was investigated by focusing on the ability of systolic blood pressure (SBP) and body mass index (BMI) percentiles during childhood, and the change in BMI percentile from childhood to adulthood to predict adult hypertension. Blood pressures in 754 adult cohort members (328 males, 426 females; mean age 44 years; range 40-49) were classified based on JNC7 criteria. Percentiles for the BMI and SBP measures obtained when these adults were closest to age 15 (mean 15 years; range 8-18) were determined based on 2000 CDC Growth Charts, and the Fourth Task Force Report, respectively. The mean SBP percentile was 62% (median 65%); the mean BMI percentile was 60% (median 62%). The mean adult BMI was 29 kg/m^2. 37% of adults were classified as pre-hypertensive, 10% as having stage I or stage II hypertension, and an additional 7% were taking antihypertensive medications. The odds ratio for adult hypertension (stage I + stage II + medications) from a multivariable logistic regression model were as follows: a 10% higher SBP percentile at age 15 OR = 1.23 (95% CI 1.13, 1.33; $p < 0.005$); a 10% higher BMI percentile at age 15 OR = 1.18 (1.08, 1.29; $p < 0.0005$); a 10% change in BMI percentile from age 15 to age 44 OR = 1.37 (1.25, 1.50; $p < 0.0001$). The odds of hypertension for females relative to males were 0.53 (95% CI 0.35, 0.80; $p < 0.005$). We also identified a significant association between *NOS3* -922A>G and hypertension at age 44. With adjustment for gender, SBP percentile at age 15, BMI percentile at age 15, and change in BMI percentile from age 15 to age 44, the odds ratios were 1.26 (0.76, 2.10; $p > 0.30$) for carriers of the variant allele relative to wild type homozygotes, and 2.20 (1.14, 4.26; $p < 0.025$), for homozygotes for the variant allele relative to wild type homozygotes (model $p < 0.0001$). Longitudinal data from The Muscatine Study demonstrate that elevated childhood blood pressure levels persist into adulthood and that children who have elevated SBP and whose BMI percentile also increases between childhood and adulthood have an even greater risk of adult hypertension. These observations again highlight the importance of obesity prevention beginning in youth if the incidence of cardiovascular endpoints is to be reduced.

Nutrition, child growth and chronic disease prevention in transitional countries

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The rising trends of obesity affecting children and adults in transitional countries can mainly be attributed to the progressive changes in diet and physical activity. Both prenatal and early postnatal factors are potential determinants of the observed trends in obesity and associated chronic disease in later life. The intrauterine environment as a conditioning factor for macrosomia and growth restriction can be a risk factor for later obesity and the metabolic syndrome; the effect of birth weight on risks follow a J or U shaped function. Childhood stunting and obesity may co-exist in populations living under conditions of poverty; while in middle income developing and industrialized countries, there is an association between tallness and high BMI. Secular trends in Chile, a post-transitional country, demonstrate that both stunting and tallness are associated with obesity; however the effect of tallness has become progressively greater. There is increasing evidence that postnatal nutritional status and growth velocity can also affect later obesity risk. Providing complementary foods to young children with the worthy objective of preventing malnutrition without considering the need to avoid obesity in stunted children may in fact do potential harm. Nutrition programs addressed at preventing malnutrition, may have built in mechanisms that can easily promote positive energy balance and thus increase risk for obesity. This is particularly relevant when feeding underweight stunted children who may be of normal or even excessive weight for stature. Thus, the importance of defining what is normal weight and height and applying normative standards to assess growth and to establish energy intake recommendations that are consistent with good nutrition and health during childhood and beyond.
Our analysis indicates that intervention strategies to address malnutrition in developing and transitional countries should focus on preventing stunting and improving linear growth rather than achieving accelerated weight and BMI gain.

Risk factors of cardiovascular traits identified in birth cohorts

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Many cross-sectional studies on the possible causes and markers of the most important chronic diseases have been carried out, but there are fewer prospective general population based studies from pregnancy exploring the risk for or protection from a disease or their intermediate risk factors, traits, until adult or old age. There is accumulating, although originally disputable, evidence from large samples that prenatal and early childhood factors really predict both cardiovascular disease (CVD) events and levels of intermediate cardiovascular disease risk factors. We have recently conducted profound parallel studies on several European populations followed from pregnancy (or birth) and shown that the pattern of early life factors on the evolution of CVD disease risk was very similar in all these cohorts despite the different ages of the cohorts and countries of origin. Generally, lower (and in some cases also higher) birth weight as an outcome of poorer intrauterine growth, even after multiple adjustment for potential confounders, associated with more adverse cardiovascular traits (higher blood pressure, insulin and some of the lipid levels, greater central fat) in childhood and later life. This was also the case for other measures of growth like postnatal catch-up growth, though the associations were less consistent. The relationships are, however, sometimes more complex, and exhibit e.g. a curvilinear shape. These varying types of association are at least partly explained by the different biological mechanisms involved and to some extent by genetic factors. The "magnitude" of risk for or protection from disease is affected by multiple factors, and especially in longitudinal studies, which have been continuing for decades, the analyses are complex and require new approaches/tools. There is still debate as to whether there are critical early periods when the effect of adverse exposures is even more harmful than during some other periods of life: does excess weight gain or non-optimal dietary habits during infancy or childhood have a greater impact on long-term disease risk than later exposure? Rising rates of overweight and other adverse metabolic disorders in children now calls for efforts towards the identification of childhood and later life-course factors that predict risk of subsequent adverse metabolic outcomes. For these purposes birth cohorts with adequate follow-ups are an ideal resource. We hope that early identification of childhood metabolic disease risk will be aided by identification of genes that regulate foetal nutrition/development, appetite, and intrauterine and later growth. We can expect that all this information can lead to targeted early prevention programs for children and families. There are good examples that we should not take it for granted that parents of young children are aware of what is a healthy lifestyle for their children.

Blood pressure in children as a risk factor for cardiovascular diseases

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Blood pressure increases as the child grows and the distribution of blood pressure values skews to the right. This has been thought to demonstrate that development of hypertension starts already in childhood. Yet the definition of hypertension in childhood is difficult. Blood pressure varies a lot and tracking of blood pressure is not stable especially before puberty. Hypertension can not be defined on the basis of normal distribution, i.e. those with values mean + two standard deviations have hypertension. This would mean that even some of the newborns would have hypertension. Because of the variability of blood pressure it is not known which blood pressure values predict the development of chronic hypertension or increase the probability to have serious cardiovascular events in adulthood.

True hypertension requiring treatment during childhood is secondary in nature, relating most commonly to kidney diseases. The prognosis of these patients depends solely on the kidney disease and thus the significance of the treatment of hypertension can not be evaluated.

Weight Control in Children

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Overweight in childhood is associated with multiple risk factors for cardiovascular disease in children and adolescents. Among overweight 5-10 year old children in Bogalusa, Louisiana, 60 % had at least one additional risk factor for cardiovascular disease, such as elevated insulin of glucose, blood pressure, or lipid levels, and 60% had two or more of these risk factors. The rapid increase in overweight children and adolescents in the last 25 years in the United States suggests that effective weight control may be the most effective strategy to reduce risk factors for cardiovascular disease in children and adolescents. A recent study of drug therapy combined with diet and physical activity demonstrates that as in adults, weight loss in pediatric patients is associated with a reduction in cardiovascular disease risk factors. Because approximately 18% of children and adolescents are overweight, clinical approaches to weight control should augment public health approaches in schools and communities. In primary care settings, rapid innovation through shared experiences has occurred. The most systematic of these efforts was implemented by the Maine Youth Obesity Collaborative (MYOC) under the auspices of the Maine chapter of the American Academy of Pediatrics. MYOC successfully applied the Chronic Care model to revise assessment and practice related to the care of overweight children and adolescents in 12 primary care practices. For example, the frequency with which BMI was measured increased from approximately 40% to over 90% over a period of 15 months. Furthermore, MYOC developed a useful algorithm for the assessment and care of overweight children and adolescents. The strategies employed by MYOC have now spread rapidly to several other collaborating groups in the states of New Mexico, Massachusetts, and Delaware. Because 2-8% of adolescents have a BMI $\geq$ 99%-tile, and because these patients are at high risk for multiple cardiovascular disease risk factors, effective care for severely overweight children and adolescents is urgent and represents a significant challenge. Primary care approaches represent a starting point for the care of these patients, but severely overweight patients may require more aggressive care, such as restrictive dietary therapy, drug therapy, or bariatric surgery. Few tertiary care centers in the United States are experienced in the provision of such care. Although revised recommendations of an expert committee for the care of overweight children and adolescents will soon be published, the development of providers and tertiary care centers capable of providing such care must become a major focus of training and practice. Finally, few clinical approaches to treatment or prevention are likely to succeed without changes in food choices or opportunities for physical activity in schools and communities. Several multi-component school and community-based programs have demonstrated reduced weight gain or decreased prevalence of overweight among children and adolescents.

The Relation of Multiple Risk Factors to structure/function of the Cardiovascular system in Youth - The Bogalusa heart Study

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The occurrence of cardiovascular (CV) risk factors in childhood has now been well established by Pediatric epidemiology studies, especially by the Bogalusa Heart Study, the Muscatine Study and Cardiovascular Risk in Young Finns Study. Risk factors in the young are predictive of adult levels and, as in adults, multiple risk factors occur commonly. These clustering in childhood are consistent with the condition of metabolic syndrome and insulin resistance. The long term persistence of multiple risk factors create an excess burden on the CV system. Most conclusive of the effect of multiple risk factors on the CV system are shown by autopsy studies. Increasing numbers of risk factors are associated with increasing severity of atherosclerotic fatty streaks and raised, collagen-covered plaques in the aorta and coronary vessels. Other measures of adverse CV changes in the young are observed in terms of greater carotid intima media thickness (IMT), loss of carotid elasticity, and increased vascular stiffness measured as pulse wave velocity. Obesity in childhood is a major characteristic predictive of adult CV disease. Greater changes occur in males than in females, and in blacks than in whites. Parental history of CV disease also contributes to sub-clinical CV disease and its risk factors in offspring. These observations underscore the importance of identifying CV risk factors and beginning prevention in childhood.

Lessons from the Cardiovascular Risk in Young Finns and the STRIP studies

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The Cardiovascular Risk in Young Finns Study was planned in 1978 according to the outlines recommended by WHO. Special attention was paid to other on-going studies (e.g. the Bogalusa Study) to be able to produce comparable data. Two pilot studies were carried out in 1978 and 1979. The first cross-sectional study was carried out in 1980 with age cohorts 3, 6, 9, 12, 15 and 18 years. In 1980 3.596 subjects were studied from East Finland (Kuopio and Oulu areas) and West Finland (Helsinki, Turku and Tampere areas). Follow-up studies have been repeated in full in 1983, 1986 and 2001 (Raitakari et al, JAMA 2003). The main purpose of the study has been to obtain data of risk factor levels and their determinants, collect background data for intervention studies and especially in 2001 to study how the risk factors in childhood and in young adulthood relate to surrogate endpoints on atherosclerosis.
Serum cholesterol and LDL-cholesterol have decreased during 1980-2001. BMI and other indices of obesity and metabolic syndrome have increased especially between 1986 and 2001. Childhood risk factors predict independently adult common carotid IMT. The next follow-up will be performed in 2007 when the participants are 30 to 54 years of age.

The Special Turku coronary Risk factor Intervention Project for children was started in 1989 (Lapinleimu et al, Lancet 1995). 1062 infants were randomized into an intervention group (low-saturated fat, low-cholesterol diet) or a control group) at 7 months of age. Serum cholesterol concentration has been 0.2-0.3 mmol/l lower in the intervention boys than in the control boys. Counselling has had no harmful effects on children's growth. Intervention is associated with enhanced endothelial function in boys (Raitakari et al, Circulation 2005). The children are now reaching 17 years of age. In recent years, the study has been expanded by inclusion of measurements of risk factors, genetics and vascular ultrasound in children's parents and grand parents.

Theory and practice of promoting healthful lifestyles in response to environmental and intrapersonal challenges

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The cornerstone of tobacco, alcohol, drug abuse, and obesity prevention, and much other health promotion research for the last quarter century has been population level experimental trials designed to assess the impact of particular approaches generally driven by one or a combination of theories about social interaction, persuasion, human learning, and/or motivation. Most of the research has been about main effects – demonstrating that a complex program results in some targeted risk factor(s) reduction. The results have been mixed, often demonstrating partial and short duration effects that have sometimes proved not to be replicable. The argument has been made that what is needed is sufficient input to achieve a tipping point, and that population interventions sometimes fall short of this. In some sense, this is bound to be true. But quantifying the ingredients and mass of input necessary to achieve tipping point is illusive. Despite the frequently reached conclusion that interventions need to be informed by an understanding of what might be at work in the prevention 'black box', little has been done to test what works inside that box, and even less has been done to assess which of the many potential factors in the social and physical environment outside the box might influence a program's effectiveness. While main effects trials have been useful, no doubt improving our capacity to bring about reductions in population risks, more research and theoretical development is needed about the mediators of program effects (inside the box) and the moderators of program effects (outside the box) to achieve broader and more durable health promotion effects. This paper reviews some of the key findings and important gaps in prevention science, particularly as they relate to explicating the need for systematic, multi-level transdisciplinary research in health promotion effect mediation and moderation. Finally, the outline of a transdisciplinary model that considers in-the-box dispositional and genetic influences and out-of-the-box environmental influences and their interactions is presented to guide future health promotion theoretical and research development.

Prevention of cardiovascular risk factors in developing countries

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Cardiovascular risk factors are rising rapidly in most developing countries. These changes are propelled by progressive urbanization, industrialization and globalization. As chronic disease epidemics advance, the poor, the young and the women are increasingly becoming the vulnerable victims. A comprehensive public health response needs to integrate both educational and policy based interventions to enable people to make and maintain healthy living choices. Policy interventions such as tobacco taxation and food pricing are likely to have a major population wide impact in a short time frame, even as education and health literacy permeate across the society to influence individuals. Such interventions are especially needed to protect the health of children and adolescents from adverse social influences, including inimical commercial interests.

Experience of school based interventions in India shows that participatory programmes, which actively involve teachers and students, are effective in reducing tobacco use. Informed health advocacy by students empowers them to become agents of social change and enhances their commitment to health promoting policies and practices. 'Learning the Fact' and 'Learning to Act' are the major components of the HRIDAY-SHAN programme of youth empowerment for health (www.hriday-shan.org). The recently concluded Global Youth Meet on Health (GYM 2006) and the launch of the Youth For Health (Y4H) movement augur well for youth led health promotion in the developing countries.

New developments in smoking prevention

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An important new development in health education is the utilization of expert systems. In stead of providing general information, these systems aim to provide a person with information that is highly tailored to the needs of the receiver. Recent research has shown that these expert systems – or computerized tailored programs as they are also called – have the potential to reach many persons. In this presentation I will provide an overview of core elements of computerized tailoring principles in general, and will discuss the results of some programs that we have developed.
Additionally, I will discuss some recent findings of 6 European countries. These results suggest that the basic assumption of smoking prevention programs may need some adjustment. One important basic assumption for the development of smoking prevention programs is that youngsters need to have resistance skill to refuse pressure to smoke. However, these assumptions are often based on cross-sectional results. Our longitudinal data suggest that selection principles may be at least as important. Furthermore, in some countries we find suggestions for parental and sibling influences.

Effect of school interventions on smoking in young people

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During the last decades, many smoking prevention activities for adolescents have been implemented. Prevention programs are very commonly situated in schools, because schools are very natural place to provide health education. Since prevention programs providing solely information appear to be ineffective, other prevention programs therefore have been added. Positive short term results have been achieved by non-smoking competitions. These competitions motivate adolescents to abstain from smoking for a certain period and if they succeed to do so they can win prizes. Social influence approaches use normative education methods and resistance skills training. With this approach number of studies have accomplished some short-term positive results, some long-term result have been reached as well. Also several studies indicate that with school-community incorporated program setting smoking rates can be deducted. Combination of community and school based programs seem to be the most promising in reducing smoking among adolescents.

Policies in adolescent cardiovascular health promotion

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Unfavourable lifestyle changes accompanying industrialisation, urbanisation, and increased discretionary income increases the degree of exposure to cardiovascular disease risk factors. An early introduction of a healthy lifestyle as healthy food habits, regular physical activity and refrain from the use of tobacco, is essential in the prevention of cardiovascular disease and several other chronic diseases, seeing as health behaviours track from childhood to adulthood. Therefore, a reason to target intervention strategies in children is that their behaviours may be influenced more easily than already established unfavourable habits among adults. In addition, cardiovascular disease has been shown to have its onset already at an early age and disease processes may be more effectively altered at relatively young ages.
Initiatives aimed at promoting health and preventing disease varies in scope, from measures targeting individuals or small well-defined groups to interventions targeting a whole population. Similarly, interventions can be implemented at different levels ranging from programmes directly influencing individual behaviour to more indirect interventions e.g. legislation, taxation, labelling or other health policy initiatives. The majority of interventions related to children and adolescents have been targeted at the school or family level, but there is increasing recognition that reaching the community at all levels is important for interventions to be effective.

Promoting health and preventing disease across the life-course: Issues and challenges

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While there have been considerable gains in the health of most national populations over recent decades, these have not been shared equally across the population. Consistently poorer health outcomes are evident for persons from socio-economically disadvantaged backgrounds, those who live in rural or remote locations and native populations. These disparities are generally evident across all stages of the life-course and most health indicators, and in many countries, the inequalities between the most and least disadvantaged have widened considerably in recent years. Clearly, a complex array of upstream (e.g. government policies, health care and other service systems), mid-stream (e.g. social, physical, economic and environmental contexts) and individual-level factors contribute to these disparities. Recent research has advanced our understanding of the relationship between people's living environments and health and also the ways in which a range of family, home, school and socioeconomic factors are associated with the development of health problems during childhood, adolescence and the adult years. Combined with new theoretical approaches, study designs and methods, our understanding of the determinants of health and the genesis of childhood health inequalities has increased significantly in recent years. The challenge is now to develop, implement and properly evaluate a new generation of prevention trials that appropriately address the key factors that are linked to long term risk of cardiovascular disease in young people and their families. These interventions will need to address settings including the home and family, childcare and school, parental workplace and the wider community. These complex intervention trials will need to build on the lessons learnt from community prevention trials conducted over the last 30 years.

U.S. Strategy for Cardiovascular Disease Prevention

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In the United States, the federal government's policy for heart disease and stroke prevention is based on the comprehensive decennial goals and objectives for disease prevention and health promotion, *Healthy People 2010*. The goals specific to this area are (1) prevention of risk factors, (2) detection and treatment of risk factors, (3) early identification and treatment of heart attacks and strokes, and (4) prevention of recurrent cardiovascular events. These goals are the foundation of the *Public Health Action Plan to Prevent Heart Disease and Stroke*, a long-range strategic plan developed by CDC in partnership with many national organizations and federal and state health agencies. Goal 1, prevention of risk factors, is applicable in principle throughout the lifespan but must focus especially on childhood and adolescence. Atherosclerosis of the aorta and coronary arteries even in this early period is strongly associated with blood lipids, blood pressure, smoking, and related factors. Preventing risk factors on an epidemic scale was the essence of Strasser's concept of "primordial prevention," which has been echoed in recommendations from the World Health Organization and, in the U.S., by numerous reports from both governmental and non-governmental organizations. One specific intervention that illustrates this aim is CATCH (Coordinated Approach to Child Health), a school-based physical activity, nutrition, and smoking prevention program. Implementation of the *Action Plan* by the National Forum for Heart Disease and Stroke Prevention centers on the work of seven Implementation Groups, each of which has potential to address prevention of risk factors under a comprehensive action framework that will be presented and discussed. Fully implementing the *Action Plan* will require that we strike a new balance in our investment in health, putting prevention first; transform our public health agencies into effective instruments for policy and environmental change; and prevent the causes themselves of heart disease and stroke.

National and international policies to promote heart health in youth

Pekka Puska, Professor (M.D., Ph.D., M.Soc.Sc.)Director General of the National Public Health Institute (KTL)

Roots of CVD go to childhood and youth. Risk related behaviors and lifestyles are usually adopted in childhood and youth, and they tend to continue in adulthood. Thus ideal prevention and heart health promotion start in childhood and in youth. In the first place the habits followed and taught at home are crucial. Later on peers, schools, leisure time activities, community circumstances, media, commercial influences and ultimately national policies play a role. While parents, schools and health services should give children and young people the knowledge and necessary skills for heart healthy lifestyles, determined policies on local, national and international level are needed to support heart healthy choices and habits. On global level WHO has recently initiated two major policy instruments: the Framework Convention on Tobacco Control and the Global Strategy on Diet, Physical Activity and Health. They both give excellent frameworks for effective national and local policies to promote heart health also in youth. Different aspects of such policies will be discussed.