Emergence of Western diseases in the tropical world: the experience with chronic cardiovascular diseases

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Our knowledge of the disease burden components of tropical populations is fragmentary. Historically, the infectious diseases have been emphasized but, as some populations have undergone socio-economic changes, vital statistics have described a change in the pattern of disease. The picture is of a decline in infectious and a rise in chronic non-communicable disease. We focus here on the emergence of chronic cardiovascular diseases, and use hypertension as the paradigmic example.

Early blood pressure surveys showed a virtual absence of hypertension among rural Africans and moderate prevalences in the Caribbean. Prevalence was highest among US and UK blacks. In a recent comparative study of blood pressure and its determinants in Nigeria, Jamaica and the US there was a steep gradient in prevalence from 15% through 26% to 33%. Body mass index and salt intake were the major determinants, accounting for 70% of the variance in hypertension prevalence. Additional information on mechanism comes from the exploration of the renin-angiotensin system across these populations. Angiotensinogen levels rise steadily from Africa to the US and are modestly associated with body mass index (BMI), and even more modestly with polymorphisms of the angiotensinogen gene. 30% of the variation in angiotensin-converting enzyme levels is attributable to the insertion/deletion polymorphism, and angiotensin-converting enzyme levels are modestly related to BMI and blood pressure. Thus, the steep gradient in prevalence is not attributable to the genetics as manifested in the renin-angiotensin system.

The usefulness of these and other data on cardiovascular diseases include planning for primordial prevention in Africa and amelioration of existing epidemics in the Caribbean, the US and the UK. Additional long term surveillance data to define the burden and distribution of causes are necessary in Africa. Lastly, education and advocacy to transfer the information to policy makers and planners is required.

The components of the disease burden in the tropical world remain poorly understood and a range of formidable challenges insure that
progress will continue to be slow\(^1\,^2\). The geographic regions spread across the centre of globe are extraordinarily diverse and the health systems which serve the populations living there are often inadequately developed. Providing the ecological resources which made the development of our species possible, the fecundity of the equatorial world likewise supports an enormous variety of human parasites. Tropical medicine has, therefore, been viewed primarily as a sub-specialty of infectious disease. This tendency is no doubt enhanced by the importance placed on control of infection by European colonisers. Although the imprint of the selective pressure exerted by malaria can be clearly discerned in the genome of tropical populations, the public health record of these events is exceedingly limited\(^2\,^3\). Only the most general impressions of health status can be deduced for indigenous peoples living a traditional lifestyle in equatorial regions. In the modern era, on the other hand, a number of countries have acquired functioning vital records’ systems and the burden of disease can be described with reasonable confidence\(^3\,^4\). Although varying widely in the rate at which the transition is taking place, and the specific character of the emerging diseases, the epidemiological pattern within these countries broadly indicates a sharp decline in the importance of infections and the rise in prominence of chronic disorders (Fig. 1)\(^3\).

Given the enormous heterogeneity within the tropics, however, and the uneven quality of the evidence, it would not be possible in this context to provide a comprehensive overview of the contemporary patterns. Our attention is, therefore, restricted to regions where we have direct research experience, viz West Africa and the Caribbean. We have likewise chosen to focus exclusively on cardiovascular diseases as the paradigmatic example of emergent chronic conditions. Not only do these syndromes represent the most common cause of death worldwide among adults\(^4\), they are easier to study with current epidemiological methods.

The common cardiovascular diseases

Interest in cardiovascular diseases in Africa and the Caribbean dates to a series of early blood pressure surveys\(^5\,^6\). With a mixture of anthropological and medical interest, investigators noted the virtual absence of hypertension among rural groups in Africa\(^5\), and the apparent upward shift in blood pressure on exposure to a Westernized lifestyle\(^7\). Epidemiological surveys in the Caribbean demonstrated moderate levels of hypertension by the 1960s, although variation in technique and the age structure of the population being examined limits the precision of these comparisons\(^6\). A formal comparison between the distribution of blood pressure in The Gambia and the West Indies was also reported\(^8\).
While innovative at the time, the first generation of survey research provided only the most general outline of the evolution in cardiovascular risk that has been taking place. Additional dimensions of this problem can now be discerned given the accumulated public health record and ongoing epidemiological research. The great deficiency, of course, continues to be the knowledge base available for Africa. Despite extrapolations made from the fragmentary data available on black South Africans, the health status of adults in sub-Saharan Africa is essentially unknown. At the present time, reasonable summary estimates of the disease burden based on mortality exist for the Caribbean nations, although verification in cohort studies has only taken place in Trinidad. To extend the sociocultural gradient it is possible to use the health experience of persons of African origin in North America and the UK as an additional point of comparison, although the interpretation of these contrasts, within a historical and evolutionary context, is exceedingly complex.

Within these broad outlines it is clear that cardiovascular disease has emerged from making a relatively minor contribution to adult mortality in West Africa – probably in the range of 5–7% of deaths – to being the predominant cause in the US and the UK (Table 1). Within Africa, stroke is thought to be the most common fatal complication of elevated blood pressure, although no population-based studies verify this assertion. Renal failure and heart failure are seen frequently at health facilities, and survival with these conditions is often exceedingly short. Except among the elite segments of society, coronary heart disease (CHD) is thought to be extremely rare. In the US and the UK, of course, CHD represents the single largest cause of death. The component causes of cardiovascular disease are now well known and the risk profile for a population can predict, with a high degree of accuracy, the burden of atherosclerosis. The profile of the classical risk factors in developing countries is
Table 1  Public health statistics on chronic disease burden and life expectancy in US, Jamaica and Nigeria

<table>
<thead>
<tr>
<th>Proportion of deaths (%)</th>
<th>US*</th>
<th>Jamaica</th>
<th>Nigeria</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV</td>
<td>49</td>
<td>36</td>
<td>7</td>
</tr>
<tr>
<td>Cancer</td>
<td>23</td>
<td>15</td>
<td>4</td>
</tr>
<tr>
<td>Diabetes</td>
<td>4</td>
<td>11</td>
<td>0.5 (7)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Life expectancy (years)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>69.2</td>
<td>74</td>
<td>50</td>
</tr>
<tr>
<td>Women</td>
<td>67.9</td>
<td>71</td>
<td>?</td>
</tr>
</tbody>
</table>


generally characterized by a diet low in animal products, low levels of serum lipids, and moderate cigarette use. Hypertension, therefore, contributes the most prominent risk to cardiovascular health.

Interest in hypertension research can be divided into three main categories. Descriptive studies which define the prevalence of hypertension and its associated disease burden are crucial to informed public health policy. An understanding of the etiology of hypertension, by the combined study of risk factors, genes and pathophysiology, forms a central task of researchers in this field. Finally, to be successful, strategies to prevent and control hypertension must be based on a solid base of empirical evidence.

Hypertension: prevalence and risk factors

Populations derived from West Africa present a unique opportunity to characterize the range of hypertension risk (Fig. 2). Prevalences in rural Nigeria and Cameroon remain among the lowest observed in human societies, with the exception of non-literate isolates (Table 2). By contrast, among blacks in the US and the UK, hypertension prevalences are at the upper extreme\(^{10}\). A marked urban-rural gradient can be documented in Africa, reflecting the second stage of the social transition. In the Caribbean, hypertension occurs among 20–25% of the adult population and represents a significant public health problem.

Our ability to characterize causal risk factors for hypertension is limited – epidemiological measures explain no more than 15% of the inter-individual variance in blood pressure. Relative weight, usually characterized as body mass index (BMI; weight/height\(^2\) usually in kg/m\(^2\)), is the most reliable correlate of hypertension, and marked differences are seen among populations of the African diaspora (Table 3). As might be anticipated at the population level, the average BMI bears a close
Fig. 2 The relationship between prevalence of hypertension and mean body mass index among seven populations of West African origin.

relationship to hypertension prevalence (Fig. 3). Clearly BMI serves as a marker for multiple life style attributes, including physical activity, sodium intake, diet composition, economic position, etc. Furthermore, the physiological pathway through which obesity mediates the associated rise in blood pressure is unknown. Emerging evidence suggests that lean body mass, which is highly correlated with body size, may play the determining role. Further analyses suggest that the slope of blood pressure with BMI is not entirely consistent across population groups. In rural Nigeria, for example, the average increase in blood pressure with increase in relative weight is twice that observed in the

Table 2 Prevalence of hypertension by gender in three populations of West African origin

<table>
<thead>
<tr>
<th>Site</th>
<th>Hypertension*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
</tr>
<tr>
<td>Nigeria</td>
<td>6.9</td>
</tr>
<tr>
<td>Jamaica</td>
<td>13.0</td>
</tr>
<tr>
<td>US (Maywood)</td>
<td>23.1</td>
</tr>
</tbody>
</table>

*Hypertension: systolic BP ≥ 160 or diastolic BP ≥ 95 or taking anti-hypertension medications; age-adjusted.
Fig. 3 The prevalence of hypertension among seven populations of West African origin.

Table 3 Body mass index and waist-hip ratio in men and women from Nigeria, Jamaica and US

<table>
<thead>
<tr>
<th>Site</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Body mass index</td>
<td>Waist-to-hip ratio</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Nigeria</td>
<td>21.7</td>
<td>3.6</td>
</tr>
<tr>
<td>Jamaica</td>
<td>23.4</td>
<td>4.0</td>
</tr>
<tr>
<td>US (Maywood)</td>
<td>27.1</td>
<td>5.5</td>
</tr>
</tbody>
</table>

urban area. These interactions, occurring in what is thought to be the best characterized risk variable, raise a note of caution for cross-cultural comparisons of blood pressure risk factors.

Sodium intake plays a fundamental role in conditioning risk of hypertension. In Nigeria, at the present time, virtually no difference in rural and urban intake of sodium occurs among those segments of the population which consume the local diet; potassium, however, tends to be lower in the urban areas, reflecting, most likely, the availability of fresh fruits (Table 4). In the Caribbean islands, sodium intake has increased relative to Africa, and a further substantial upward step occurs in North America. Whether sodium interacts with obesity and other risk factors to accelerate the age-related rise in blood pressure seen in these groups is unstudied as yet.
Considerable scientific interest has been focused on the role of psychosocial factors in determining hypertension risk. A well known study in Kenya documented a prompt rise in blood pressure among Luo residents who migrated to Nairobi\textsuperscript{14}. Unfortunately, no reliable methods exist at the present time for measuring the putative exposure directly. It would appear to even the casual observer that the pace of life varies enormously in the village and in the city; whether this correlates with predictable psychological effects is much harder to know. In the Kenyan study, pulse rate was shown to be elevated, although the validity of this measure has never been well demonstrated. In Nigeria, self-reported levels of individual social support were found to relate to blood pressure, particularly among women\textsuperscript{15}.

As might be anticipated, life style risk factors related to hypertension tend to emerge in a consistent pattern as the social structure changes. To date, no good evidence suggests that human populations vary in their relative susceptibility to these factors. The population attributable risk

Table 4 Urinary electrolytes among persons of West African origin

<table>
<thead>
<tr>
<th>Site</th>
<th>Sodium Mean</th>
<th>Sodium SD</th>
<th>Potassium Mean</th>
<th>Potassium SD</th>
<th>Na/K ratio Mean</th>
<th>Na/K ratio SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nigeria</td>
<td>121.5</td>
<td>76.1</td>
<td>48.9</td>
<td>26.4</td>
<td>2.7</td>
<td>1.3</td>
</tr>
<tr>
<td>Jamaica</td>
<td>143.6</td>
<td>112.6</td>
<td>54.3</td>
<td>38.2</td>
<td>3.3</td>
<td>2.4</td>
</tr>
<tr>
<td>US (Maywood)</td>
<td>172.5</td>
<td>80.3</td>
<td>49.5</td>
<td>23.5</td>
<td>4.1</td>
<td>2.5</td>
</tr>
</tbody>
</table>

British Medical Bulletin 1998;54 (No. 2)
of these exposures is, therefore, determined only by variation in prevalence. In rural West Africa, based on multiple measurements, hypertension would be relatively uncommon – occurring at a prevalence of around 5%, primarily among persons over 55 years of age.

As a framework for implementing primordial prevention, these populations are of special interest because they enjoy exceedingly good cardiovascular health. On average, members of these societies are very lean, physically active and consume only moderate amounts of sodium. However, the requirements for physical work are punishing and many individuals in these populations are undernourished. In a small scale longitudinal study, all-cause mortality in adults approached 3%\textsuperscript{16}. Practically speaking, it must be assumed that optimal health will require a transition along the spectrum to a modernized lifestyle which goes well beyond the conditions of life experienced by these subsistence farming communities – a harvest of cardiovascular disease can be anticipated. There is every reason to suspect, therefore, that, for the foreseeable future, specific, targeted strategies to prevent and treat hypertension in high risk individuals will be necessary in these societies.

**Hypertension: physiological mechanisms**

Among the best studied of the physiological pathways which control blood pressure is the renin-angiotensin system (RAS). The RAS influences blood pressure through salt and water balance, and the effect subsequently on the set point of renal perfusion pressure. Direct effects also occur at the level of vascular tissue. Abnormalities in the RAS have long been thought to underlie the propensity to hypertension, and Blacks have been characterized as having unusually low renin levels. Evidence for differences in the function of the RAS among populations of West African populations and Blacks in the Western hemisphere are virtually non-existent, however. We have recently demonstrated that angiotensinogen levels rise progressively in population samples from Nigeria through Jamaica to the US (Fig. 4)\textsuperscript{17}. Substantial variation was observed among the Black populations studied, with mean angiotensinogen increasing in a linear fashion from ~1400 (ng/ml of Ang-I generated) in rural Africa to 2000 in metropolitan Chicago (Fig. 4). Although polymorphisms of this gene influence concentration modestly\textsuperscript{18}, this cross-population trend does not appear to have a genetic basis\textsuperscript{19,20}. The impact of known genetic polymorphisms is much smaller. Mean differences between persons homozygous for methionine at position 235 compared to the complementary homozygotes was approximately 10–15% \textit{(i.e. 1300 versus 1450 ng/ml)}\textsuperscript{18}. Assuming that the contrast observed between the Nigerian and the US participants is
entirely environmental in origin, it is apparent that the range of known effects induced by genes is considerably less than that of the environment. Activity of the angiotensin converting enzyme (ACE) is another component of the RAS which has been widely investigated in recent years. While consistently related to the insertion/deletion polymorphism in the ACE gene, correlations have generally not been observed between ACE levels and blood pressure. Lastly, serum ACE does also appear to vary with BMI, although – as in most relationships within the blood pressure control systems – the magnitude of the correlation is again very modest.

**Hypertension: prevention and control**

As noted above, it is impossible to imagine at the present time a means of eliminating the emergence of hypertension as a mass public health problem for the tropical countries. Prevalences range widely, and depend on the survey methods used and the age structure of the population. Using a definition of 160/90 mmHg, most modernizing societies will experience prevalences of 5–15%. Abundant randomized trial experience demonstrates that these individuals will benefit from drug treatment. Successful treatment of large segments of the population for lifelong conditions requires an enormous investment in resources, however, and a crucial challenge to the developing countries of the tropics will be how to put in place a rational policy for medical resource allocation. To date, the tendency has been to adopt, intact, the guidelines promulgated by US and European agencies, and apply them to the affluent alone, or intermittently to the broader groups in society. An algorithm has now been developed which permits absolute risk to be used as the basis for determining blood pressure treatment threshold. With this approach, the cost effectiveness of treatment can be estimated directly, and an informed judgement made regarding the relative value of long-term drug therapy. In the meanwhile, a vigorous search for effective preventive strategies must continue.

**Prospects for the future**

As a species, we have ventured well beyond our evolutionary homeland, and the disease burden imposed by these socially mediated alterations in our environment are the principal challenges for public health. Reasoning in the opposite direction, it is clear that some chronic diseases allow an evolutionary solution while others do not. For example, a fat modified diet is entirely consistent with an acceptable lifestyle in
industrialized society, and enormous progress has been made in controlling the CHD epidemic based on that fundamental change in eating patterns. Returning to the dietary composition in force over the majority of our evolutionary history is, therefore, a potential solution. Unfortunately, no similar solutions exist for hypertension, obesity and diabetes. On average, we are programmed as a species to experience a rise in body weight and blood pressure with age under the conditions of modern life. Reducing sodium intake to 10 mmol, as among the Yanomami, or maintaining high levels of physical fitness and the associated absence of obesity, as among rural Nigerians, cannot be accomplished at the present moment. Pharmacological interventions, perhaps the most extreme form of a non-evolutionary solution, have emerged as a mass public health strategy only for blood pressure control.

In this perspective the challenges of vascular disease in the tropics are no different from any other modernized segments of the world. The more urgent question, however, is whether the lessons learned in North America and Europe can be applied successfully to the tropical world, and forestall the coming epidemics. While the general biological principles are surely the same, the social conditions under which they are operating are very different. Local modifications of preventive strategies will be necessary. Several essential ingredients of a public health programme which will be required to achieve this goal can now be identified. Long-term, community-based surveillance projects are needed to define the burden of chronic disease among adults – both the distribution of causes and outcomes. An educational effort will be required to transfer what has been learned about chronic disease epidemiology to physicians and policy makers in these countries. Availability of new tools, including molecular biology, will provide important resources for local investigators in areas ranging from diagnostics to etiological research. A health services agenda which includes the development of effective methods of treating chronic disease will also need to be formulated and supported. Finally, as the essential long-term goal, integrated research on human biology must be successful if we are to construct either evolutionary or non-evolutionary preventive strategies.

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