Hypertension in Sub-Saharan African Populations

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Background—Hypertension in sub-Saharan Africa is a widespread problem of immense economic importance because of its high prevalence in urban areas, its frequent underdiagnosis, and the severity of its complications.

Methods and Results—We searched PubMed and relevant journals for words in the title of this article. Among the major problems in making headway toward better detection and treatment are the limited resources of many African countries. Relatively recent environmental changes seem to be adverse. Mass migration from rural to periurban and urban areas probably accounts, at least in part, for the high incidence of hypertension in urban black Africans. In the remaining semirural areas, inroads in lifestyle changes associated with "civilization" may explain the apparently rising prevalence of hypertension. Overall, significant segments of the African population are still afflicted by severe poverty, famine, and civil strife, making the overall prevalence of hypertension difficult to determine. Black South Africans have a stroke rate twice as high as that of whites. Two lifestyle changes that are feasible and should help to stem the epidemic of hypertension in Africa are a decreased salt intake and decreased obesity, especially in women.

Conclusions—Overall, differences from whites in etiology and therapeutic responses in sub-Saharan African populations are graded and overlapping rather than absolute. Further studies are needed on black Africans, who may (or may not) be genetically and environmentally different from black Americans and from each other in different parts of this vast continent. (***Circulation*. 2005;112:3562-3568.)**

Key Words: hypertension ■ epidemiology ■ blood pressure

"*Africa provides a vast natural laboratory for the study of the etiology and epidemiology of heart disease*" (Bradlow et al[1]).

In 1929, an article in *The Lancet* described blood pressure (BP) patterns in an Africa community living in "conditions which have probably undergone no appreciable change for many centuries," Donnison wrote. "Over two years at a native hospital in the South of Kavirondo in Kenya, during which period approximately 1800 patients were admitted, no case of raised blood pressure was encountered, although abnormally low blood pressure was not uncommonly encountered. On no occasion was a diagnosis of arteriosclerosis or chronic interstitial nephritis made."[2] He pointed out that similar BP patterns were to be found in Africans and Europeans until ≈40 years old, after which BP rose in the European but not in the African. He contrasted the unchanged pattern of existence for a large number of generations in this nonindustrial and tribal African group with the "revolutionary changes in their mode of living" of the Europeans and blamed greater mental stress for their higher BP. Today, more than 75 years after Donnison, when change has been sweeping through Africa, extensive epidemiological studies show that hypertension is one of the commonest cardiovascular ailments in Africa and that BP assumes much more importance with increasing age.[3,4] Furthermore, the increasing incidence of diabetes in Africa[5] will augment the severity of renal and cardiac damage caused by any given BP level. Overall, the total number of hypertensives in the developing world is high, and cost-analysis shows that these countries cannot afford the same treatment as developed countries.[6] Although the present article focuses on sub-Saharan Africa, hypertension is equally a problem in the supra-Saharan countries such as Egypt.[7]

Urban Versus Rural Trends in Africa

Several studies attest to rural versus urban differences in BP levels throughout sub-Saharan Africa.[8] The prevalence of hypertension (BP ≥160/95 mm Hg) in rural studies undertaken in the 1970s, 1980s, and 1990s has generally been low: 4.1% in Ghana,[9] 5.9% in Nigeria,[10] 7% in Lesotho,[11] and 9.4% in the rural Zulu.[12] In the latter group, the onset of hypertension measured by an aneroid sphygmomanometer was delayed compared with their urban counterparts.[12] In the tribal South African Xhosa[13] and in the San tribes (previously called Bushmen) living in the desert as hunter-gatherers and subsisting only on game and wild vegetation,[14] BP levels were relatively flat with age. Much depends on the definitions of hypertension used and the anthropological groups under

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study. In Cameroon, the rural age-adjusted prevalence of hypertension measured by mercury sphygmomanometer was ≈5.7% according to the "old" definition (160/90 mm Hg) but was 13% in men and 9% in women according to the new criteria (140/90 mm Hg).[15] By 2001 to 2002, the incidence of hypertension at the new lower values, as measured by the OMRON sphygmomanometer, rose considerably with age in a Ghanaian rural community, with approximately one third being hypertensive at age 65 years or more.[4] Such changes are probably the result of acculturation,[16–19] which can be expected to proceed at different rates in different rural communities. Thus, the migration of people from traditional rural areas on the northern shores of Lake Victoria to the urban settings of Nairobi was associated with an increase of BP (as assessed by the random-zero sphygmomanometer). The urban migrants had higher body weights, pulse rates, and urinary sodium-potassium ratios than did those who remained in the rural areas.[16] This suggests a marked change in diet of new arrivals in Nairobi, with higher salt and calorie intake and a reduced potassium intake. The higher pulse rates in the Nairobi participants also suggest that increased autonomic nervous system activity could contribute to the higher BP levels[16]

A reasonable hypothesis is that more urban societies have a higher risk of hypertension when compared with the more rural. The data of Cooper et al,[21] who used a Dinamap sphygmomanometer to assess age-adjusted hypertension, showed a prevalence of 15.4% in rural Cameroon and of 19.1% in urban Cameroon. More recently, in 2004, in tribal villages in Ghana, the levels of hypertension (BP ≥140/90 mm Hg, measured by automatic monitoring or antihypertensive therapy) in those >65 years old, was ≈37% versus ≈50% in the semiurban dwellers.[4] There may be important differences between the nonindustrialized, isolated rural tribes (as still exist in parts of Africa) and the semiurban, the latter now under more pressure from "civilization."

Comparisons With Black Americans

In a large US study, the prevalence of hypertension was evaluated between 1988 and 1991. The National Health and Nutritional Survey (NHANES) showed that overall, hypertension was more common in blacks (32%) than in whites (23%) but by the seventh decade of life, BP levels were similar.[22] The authors did not comment on this discrepancy, but a possible explanation is that more severe hypertension in younger blacks led to a greater mortality rate, leaving less severely afflicted black hypertensives to age. The higher prevalence and severity of hypertension in black Americans have multifactorial origins,[23] rather similar to those proposed for blacks living in Africa (see next section). A major risk factor for hypertension is obesity, which can account for differences in the standardized hypertension prevalence of ≈16% in West Africa, ≈20% in urbanized West Africans, and 26% in the Caribbean compared with 33% in the United States.[24] These data, collected from 1991 to 1994, led Cooper et al to opine that "rural Africa remains one of the social environments that is kindest to the human cardiovascular system."[24] Unfortunately, it seems as if by 2001 to 2002, at least some of rural Africa was succumbing to the advance of civilization.[4]

South African Surveys

Even here, exact data are difficult to obtain. In 1983, an age-adjusted prevalence study of the adult population of Durban (World Health Organization criteria ≥160/95 mm Hg) showed that hypertension was highest in urban blacks of the Zulu tribe (25%), intermediate in whites (17%), lower in ethnic Indians (14%),[25] and lowest in rural blacks (9%).[12] The first Demographic and Health Survey in South African was conducted in 1998 in a random sample of 13 802 subjects aged 15 years or older, of whom 76% were black, 13% of mixed ancestry, 8% white, and 3% India/Asiatic.[26] The age-adjusted incidence of hypertension, namely, BP ≥140/90 mm Hg on medication, measured automatically, for this predominantly black South African population was 21% (females and males had equal rates). For those >65 years of age, 50% to 60% were hypertensive. The latter figures are slightly higher than those for a similar age group in semiurban West Africa.[4] Note that there is little information on isolated systolic hypertension, essentially a disease of the elderly.[27]

Proposals on the Prevalence of Hypertension in Sub-Saharan Africa

In communities living in conditions described by Donnison in 1929,[2] BP may still stay flat with advancing age, but such groups may be dwindling rarities. Latest surveys show that by >65 years of age, the prevalence of hypertension is ≈30% to 40% in rural West Africa, ≈50% in semiurban West Africa,[4] and 50% to 60% in a mixed South African population.[26] The latter values are now approaching the 60% to 70% range for black Americans of similar age.[22] With sub-Saharan Africa's population of 650 million and increasing longevity and Westernization, hypertension has now changed from a relative rarity to a major problem. "Ten million to 20 million may be affected in sub-Saharan Africa; the African Union has called hypertension one of the continent's greatest health challenges after AIDS."[28] However, what is not known is what proportion of the African population lives in truly rural conditions, relatively immune to the "advances" of civilization, versus those succumbing to urbanization either rapidly or gradually. Nor is it easy to factor in the influence on hypertension prevalence of the growing number living in abject poverty and famine promoted by climate change and persistent droughts, sometimes complicated by civil strife. Thus, the aforementioned estimates may be too high. Another evolving factor to consider that may be widespread in Africa is the shortened life span, as now established in South African blacks, due to the HIV/AIDS epidemic, which both eliminates the normal age-related increase in BP and also predisposes to underweight and malnourished orphans, eventually leading to a long-term decline in general health and increasing poverty.[29] Life expectancy at birth is projected to decline during 2001 to 2006, from 54.8 to 46.9 years during 2006 to 2011 to 44.7 during the period 2011 to 2016.[29]

Hypertension in Sub-Saharan Black Populations

Incidence	Lower in Rural Blacks, Increasing With Urbanization; Becoming Similar to Black Americans
Multiple causative factors	Lower plasma renin
	Sodium abnormalities
	Epithelial sodium channel changes
	Altered genes regulating the RAAS
	Increased peripheral vascular resistance
	Increasing obesity
	Socioeconomic stress
	Underweight phenotype
Trends in therapy	Low-dose diuretics
	CCBs
	Less response to ACE inhibitors, β-blockers, and clonidine as first-line agents
	Compelling indications need specific drugs, eg, ACE inhibitors for diabetic nephropathy and renal disease

Are There Ethnicity-Related Causes of Hypertension?

In considering sub-Saharan Africa, undoubtedly the vast majority of the population can be defined as black. Proposals about hypertension in black Americans may not relate to Africans living in Africa who have never emigrated, nor need these proposals apply to other Africans of different tribal or genetic origins living elsewhere in Africa; eg, West Africa may differ from South Africa, Zimbabwe, or Kenya. Thus, any statements about the origins of hypertension in relation to one group of Africans may not apply to any other. Although black Americans or other black populations may be more vulnerable to hypertension and may even have different causative factors or different degrees of the same causative factors, such as obesity, "their genetic predisposition may be permissive rather than determinative,"[30] requiring biosocial factors such as weight gain, a high salt intake, or anxiety, and psychosocial stress or excess alcohol consumption to precipitate the disease.[20,25] Bearing in mind all of these reservations, the following aspects of etiology are hypothesis generating rather than definitive. Multiple mechanisms may be at work (Table).

Low Plasma Renin Values

Although it is generally believed that a low plasma renin value is typical of hypertension in the ethnic black population, this is not a distinct characteristic of hypertension, at least not in black Americans.[31] Rather, there is a broad range of values. Overall, a black hypertensive is more likely than a white hypertensive to have low renin values, with many in both groups overlapping in the medium range. Likewise, although South African blacks respond less well to angiotensin-converting enzyme (ACE) inhibitor therapy than to calcium channel blockers (CCBs), as discussed later, the explanations may be complex.[32] Differences in renin levels may at least in part be environmental in origin, in that low renin values have been found in South Africa in urban but not in rural Zulu populations and also in urban Natal Indians.[33] Of note, sodium restriction in black Zimbabweans did not increase plasma renin values in hypertensives but, as expected, elevated the value in controls.[34] Among the explanations for the strong trend to low renin values are abnormalities of sodium handling, such as excessive sodium renal reabsorption, and genetic abnormalities in the renin-angiotensin system or related genes. With regard to angiotensinogen, levels in Nigeria are substantially lower than those in the US black population, but these differences chiefly reflect obesity, sex, and age.[35]

Sodium Sensitivity and Cellular Abnormalities

Sodium levels in circulating blood cells are high in South and Central African hypertensive blacks,[36,37] with depression of the sodium pump.[38] Cell sodium levels are higher in hypertensive than in normotensive South African Zulus,[39] especially in association with the BP rise.[33] On urbanization of Kenyan blacks, the urine sodium-to-potassium ratio consistently rose,[17] suggesting an increased dietary sodium intake. In black urban South Africans, the sodium pump defect was linked to low cellular magnesium levels.[40]

Epithelial Sodium Channels

Whereas a positive correlation might be expected between plasma renin and aldosterone, its absence in South African urban Zulus and Indians suggests an environmentally induced defect.[33] In a pilot study of a subgroup of South African blacks, a new mutation (R563Q) of the β-subunit of the epithelial sodium channel was found to be associated with low-renin, low-aldosterone hypertension.[41] Closely related is the increased transepithelial sodium absorption found in black persons living in London when compared with white counterparts.[42] However, this is not a specific gene variant but rather describes a general trend found in the black group.

Genes Controlling the Renin-Angiotensin-Aldosterone System

Although it is renin and not angiotensinogen that is normally thought to be rate limiting for the renin-angiotensin-aldosterone system (RAAS) and hence, the major switch-on signal, abnormalities in the angiotensinogen gene may be important, especially in the presence of low plasma renin activity. However, a large American study failed to find a role for the angiotensinogen-6 polymorphism in different ethnic groups.[43] In black South Africans,[44] polymorphism of the promoter region of the angiotensinogen gene ($-20A\rightarrow C$) causes a greater-than-expected rise in systolic BP for any given body mass. Polymorphism of the aldosterone synthase gene, CYP11B2, is linked to a higher initial systolic BP in previously untreated black South Africans.[45] More of such studies are under way and may uncover other genetic changes in the enzymes controlling the RAAS system.

Increased Peripheral Vascular Resistance

This factor is often thought to characterize hypertension in black Americans but has been little studied in blacks in Africa. The increase in total peripheral resistance in response

to exercise is more prevalent in urban than in rural South African blacks, suggesting environmental factors at work.[46]

Obesity

Increasing obesity is associated with increasing BP levels in West African and American blacks.[21] In the South African Demographic and Health survey of 1998, the incidence of obesity (body mass index $\geq$30 kg/m^2) in blacks was $\approx$30% in females and 8% in males, with other sample populations having rates as high as 40% to 49% in women and $\approx$13% in men.[47] Abdominal obesity was particularly common in females. "The more urbanized these communities were, the higher the rate of obesity and the less prudent their diets became."[47] Presumably, the lower male prevalence relates in part to the much higher rate of heavy manual labor.

Socioeconomic Status

In Tanzania, in 9254 urban inhabitants of Dar-es-Salaam, socioeconomic status was inversely related to BP and smoking, whereas increasing affluence was linked to increased obesity.[48] African urbanization is associated with inevitable stress, dietary changes, and acculturation, as already outlined.

Underweight Phenotype

In economically disadvantaged South Africans of mixed ancestry, low birth weight is associated with adult glucose intolerance and higher BPs, the possible result of early activation of the cortisol axis.[49]

Conclusions on the Origins of Hypertension in Sub-Saharan Africans

Apart from the putative roles of the epithelial sodium channel and abnormalities in angiotensinogen and aldosterone synthase genes reported in black but not white South African hypertensives, there are, on the whole, no major genetic differences to account for these observations, and environmental differences may account for much. Further genetic studies are ongoing. "Is it simply a heavier dose of risk factors, or do genes play a key role? We would argue that the only defensible position is one of studied uncertainty."[50] That position seems much the same now as it was 10 years ago. Perhaps both risk factors and genes contribute to the problem.

Clinical Features

In the South African black population, hypertension has typically behaved "in an explosive manner with death occurring frequently from cerebral hemorrhage, uremia or congestive heart failure."[51] With urbanization, these patterns may be changing. Although malignant hypertension is now rare among whites in the developed world,[52] it remains a common problem in developing countries, being the diagnosis in 57% of essential hypertensives in 1 hospital-based South African series in 1990.[53] This poor outlook for black patients could be explained by their late presentation and the high incidence of renal impairment. Moreover, follow-up and control of BP are inadequate because of poor education and inability to understand the severity of the illness, or the required facilities may be lacking.[52] Fibrinoid necrosis of the kidneys was found in 92% of the autopsy sections from South African blacks with malignant hypertension.[54] Data from the South African Dialysis and Transplantation Registry show that hypertension was responsible for 35% of end-stage renal failure in blacks in 1990.[53] In Nigeria (and elsewhere), diabetic nephropathy with hypertension is coming to the fore as a cause of end-stage renal failure.[55] To lessen the morbidity and mortality of this and other dreaded complications requires better BP control, attention to comorbidities, and a concerted national policy, as proposed in Nigeria.[56]

In the mid-1970s, the frequency of cardiac involvement in 1000 South African patients (500 blacks and 500 Indians) was studied for a period of 7 years.[51] Although congestive cardiac failure due to hypertension occurred in 16% of blacks, ischemic heart disease did not occur, in contrast to the much higher frequency in Indian patients.[51] Yet hypertension is commonly associated with atheromas of cerebral arteries and of the aorta.[57] In black South Africans, the relatively low blood total cholesterol values and relatively high levels of HDL[18,58,59] may help in coronary protection. In a Nigerian study, acute left ventricular failure from hypertensive heart disease was the most common cause of sudden cardiac death, but acute myocardial infarction was rare.[60] Currently, the incidence of myocardial infarction in Africans throughout sub-Saharan Africa is probably rising,[61] and hypertension is the strongest of 6 risk factors, with an astounding odds ratio of 6.99.[62]

Stroke is on the increase with Westernization and with increased rates of hypertension and diabetes, yet truly rural populations are still relatively protected.[63,64] In a recent study of a South African semirural community, the prevalence of stroke was relatively high, with the rate of stroke disability approaching that in high-income countries.[65] Of note, a large percentage, between 30% and 50%, of stroke mortality occurs in those inadequately treated for hypertension.[63] Overall, black South Africans have a stroke mortality rate twice as high as that in whites.[20]

As urbanized African black hypertensives are now being seen earlier and treated better, attention is shifting to early disease manifestations, such as left ventricular diastolic dysfunction, with a search for cardiovascular risk factors including blood lipids, glucose, and microalbuminuria.[66] Coronary heart disease still remains relatively uncommon in sub-Saharan Africa. An increasing prevalence, expected with increasing Westernization, is already suspected and reported in black South Africans with stroke.[67]

Prevention and Treatment

Inadequate funds, inexperience, and lack of infrastructure remain important barriers to hypertension diagnosis and therapy. All reports indicate that the prevalence of hypertension is high and that 2 major problems are first, detection and, second, a "very low level" of adequate treatment.[4] Accordingly, the overall management of hypertension is as much a socioeconomic as it is a therapeutic problem. "There exists remarkably sparse reliable evidence on how governments of low-income countries can generate and sustain financing their countries health facilities."[56] Screening ideally not only detects hypertension but also is the basis for education and therapy.[68] Overall, detection and management of hyperten-

sion are such a vast problem that in any given country it becomes, at least in part, a political issue. There will often be competition for limited financial resources between hypertension and infectious diseases such as HIV/AIDS and malaria. An active approach to hypertension must be driven by the local ministry of health as well as by local hypertension societies, with support from influential bodies such as the International Forum for Hypertension Control and Prevention in Africa,[68] the World Heart Federation, local heart foundations, and the Pan African Society of Cardiology.

Lifestyle

Two important low-cost preventive measures are first, a reduction in dietary salt and increased potassium intake,[66] and second, a greater awareness of the serious implications of obesity.[48] Increased exercise,[69] decreased obesity, and cessation of smoking are all as important in black subjects as in whites in control of hypertension. In South African blacks, there is a clear relation between the degree of obesity and BP. In those with a body mass index in the obese range, African males had an age-standardized BP prevalence of 47%; in those with a body mass index in the overweight range, it was 33%; in normals, it was 19%; and for those underweight, it was only 11%.[20] Financial and cultural reservations apply to implementation of the DASH high-fruit, high-vegetable, low-salt diet, which is very effective in black Americans.[66] In Africa, one hypothesis is that the rural diet is relatively protective but is abandoned with urban exposure, with less carbohydrate and higher fat intake.[70] In West Africa, sodium restriction is feasible as a solitary measure,[71] but to achieve general application, it clearly requires persuasion at a governmental level and multiple messages from different sources, varying from the rural clinic to television. The major problem is how to get the lifestyle message across and how to implement it.

BP Cutoff Points and Risk Evaluation

In general, the first aim is to cast the net widely and to make antihypertensive medication available to as many with hypertension as possible. The second ideal is to promote current evidence-based medication with modern BP goals. With regard to low-cost therapy, the first crucial point is which cutoff BP values to use. Cooper and coworkers[35] calculate that using 160 mm Hg systolic as a cutoff point would mean that only 9 persons would have to be treated each year to prevent a cardiovascular event and 50 would have to be treated each year to prevent 1 death. Lower cutoff points, such as 140 mm Hg systolic, now regarded as ideal when economically feasible, lead to many greater numbers needed to treat. Thus, the higher cutoff levels, the more practical though less medically desirable is the policy for finance-limited African countries. The way forward out of this dilemma could be greater use of risk factor calculations for the individual hypertensive, which is a more cost-effective approach than decisions based on just the cutoff BP level.[72] In selected groups, such as those with diabetic hypertension or advanced renal disease, very tight control of BP remains essential.

Choice of Agent

The next point is which antihypertensive agent(s) to recommend as first-line therapy (Table). There have been no truly large-scale, randomized, outcome studies in black Africans. With regard to first-line agents, in a South African black, urbanized cohort of 409 subjects, 2 CCBs, a diuretic, and an ACE inhibitor were compared.[73] Monotherapy with the CCB was effective in 61% over 13 months, hydrochlorothiazide in 26%, and enalapril in only 1%. However, when enalapril was combined with other drugs at the end of the study, BP control was achieved in 78%. Addition of reserpine or enalapril to the diuretic gave 67% control. Whatever the therapy, an equal degree of left ventricular hypertrophy regression was achieved for equal BP reduction. In this study, no β-blocker was tested.[37,74,75] In a second South African study, another CCB decreased ambulatory BP and left ventricular mass, whereas enalapril monotherapy decreased neither BP nor left ventricular mass.[76] In Nigeria, diuretics appear to be less efficient antihypertensives than are CCBs.[77] Of note, combination therapy was often required.

Relevance of Studies in Black Americans

Although studies in black Americans may not be directly applicable to sub-Saharan Africans and extrapolations must be made with caution, there are some common points. First, there is an increasing emphasis on environmental rather than genetic factors to explain the higher incidence of severe hypertension in black subjects. Second, as in all hypertensives, there must be an overall evaluation of total cardiovascular risk of the individual patient.[66] Whereas this ideal policy is clearly more feasible in countries and environments with a higher level of socioeconomic development, risk factor evaluation also leads to a more cost-effective policy when selecting BP levels that warrant drug therapy in a South African environment.[72] Third, although the totality of experience in Africa and the United States[78] may suggest that preference should be given to low-dose diuretics and CCBs as initial agents in black Americans,[79] apparent black-white differences are not absolute but relative.[80] Fourth, for specific patients and for specific reasons, other agents may be preferred. For example, ACE inhibitor–diuretic therapy is chosen for renal disease and heart failure, and β-blockers for those with heart failure.[66] Of relevance is the reported success of an angiotensin-receptor blocker–diuretic combination in black American subjects.[81] By extrapolation, ACE inhibitors or other renin-angiotensin inhibitors, combined with low-dose diuretics, should be evaluated as possible first-line antihypertensive drugs in an African trial. Fifth, whatever the drugs chosen to achieve the desired BP reduction, the US experience is that effects on morbidity and mortality are very similar.[79,82] This conclusion provides a valid hypothesis for testing in sub-Saharan Africa. Finally, studies on black Americans can give valuable clues in efforts to limit the increasing prevalence of hypertension in African blacks. For example, the Bogalusa Heart Study proposed that improved intrauterine growth and lessened weight gain in adolescence could substantially reduce excess hypertension in black Americans.[83]

Conclusions

Sub-Saharan Africa contains a diversity of ethnic groups, cultures, and countries of vastly different socioeconomic status. From the available data focusing on black groups, hypertension seems more common with increasing urbanization, leaving behind a group of truly rural dwellers who still seem relatively protected. It is, however, the urbanized persons who have better access to modern antihypertensive care. Both lower-income groups (because of socioeconomic stress, lack of access to facilities, and poor diet) and higher-income groups (because of obesity, dietary excess, alcohol consumption, and lack of exercise) may be at increased risk of developing hypertension. Both individual "best treatment" and wider national policies need to be promoted.

Disclosures

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