EDITORIAL

THE GENETICS OF GHANAIAN HIGH BLOOD PRESSURE

That high blood pressure with its complications runs in families has been known for ages. "Hereditiy", said Ayman nearly 60 years ago, "is the most important known factor in the development of arteriolar (essential) hypertension". More recently Philippe Meyer has stated that 'Genetic factors have been shown to be responsible not only for hypertension but also for its complications'. What is less clear, however, is the exact genetic mechanism responsible for essential hypertension. Indeed, "the nature of the inheritance", says Page, "has often been the subject of acrimonious debate". While Platt and maintained that the condition was transmitted by a single gene behaving as a Mendelian dominant, Pickering thought a "graded, multifactorial or polygenic" inheritance best explained the observed facts. Whereas within a few years rats can be induced to manifest hypertension through genetic and non-genetic processes, humans with essential hypertension require several generations and large family studies with variable marriage patterns for a clear epidemiology (genetic or otherwise) to be worked out. Dr Jonathan H. Addy deserves to be congratulated for making use of the African larger family system with its polygamy and serial polyandry to work out the genetic epidemiology of Ghanaian familial high blood pressure. Dr Addy's thesis can be summarized as follows:

1. Essential hypertension in the Ghanaian adult is a homozygous condition (HH) and manifests itself as early as 30 years of age.

2. The adult non-hypertensive in Ghana has either no genes for hypertension i.e. has two normal blood pressure genes (NN), or one gene for normal blood pressure and the other for high blood pressure (NH).

3. Non-hypertensive parents who have children some of whom grow up to become hypertensive must be heterozygous for the gene (NH x NH).

4. The wife whose many children by a hypertensive man do not develop hypertension is likely to be without a hypertension gene (NN).

5. The non-hypertensive spouse of a hypertensive person must be heterozygous for the gene if a hypertensive offspring occurs. (HH x NH = NH, HH, NH, HH).

6. All the children of a hypertensive couple will grow up to be hypertensive. (HH x HH = HH, HH, HH, HH).

These, as Dr Addy points out, are the cardinal features of a recessive mode of inheritance. As if this observation was not significant enough
Dr Addy went on to mention another important finding viz: that the particular hypertension he described was "propranolol responsive", thus linking it to the "renin-angiotensinogen-hormonal system", thereby making it possible to "design clinical-pharmacological and biochemical tests for the identification of the heterozygote". Should such a biochemical test, or indeed gene mapping procedure, readily identify heterozygotes then anyone who has received even one hypertensive gene (NH) will be found to be "positive", asymptomatic though he may be. It should then be possible to distinguish by a simple test between two normal-looking phenotypes, the non-hypertensive hypertension-gene carrier (NH), and the non-hypertensive no hypertension-gene carrier (NN). This moves the phenomenon from recessiveness to dominance. As Clarke would put it in another context, "the trait is dominant to the normal situation, but the disease is recessive because it is necessary to have a double dose of the gene before the symptoms are manifested". Thus as our knowledge of disease increases definitions of dominance & recessiveness must alter, and the boundaries between dominance and recessiveness are rapidly being broken down as the level of observation moves towards the gene itself - and the concept of penetrance, too, is being modified in the process. A condition which, viewed at one level, is clearly recessive (HH) and at another is dominant (NH versus NN by laboratory test) can be said to display "intermediate inheritance" or "co-dominance".

So Platt can claim some victory here. But Pickering too can maintain his plurigenic stance by pointing out that other genes have been known to contribute to hypertension, not to mention the possible role of G6PD deficiency via the kidney which is one of the non-erythropoietic organs affected by this sex-linked gene found in 20-25% Ghanaian males. While it is important to note that non-hereditary causes of hypertension exist against a background of hereditary factors, Dr Addy said his genetic hypertensives became overtly hypertensive soon after reaching the age of 30. This valuable research was done with minimum funding. When more resources become available information could be collected among others, on the average daily salt intake (in mEq) per patient; adrenal responsiveness to angiotensin II on a low sodium intake; renal vascular responsiveness to angiotensin II on a high sodium intake; angiotensin II levels versus sodium intake; categorisation of hypertensives into low renin, normal renin, high renin groups; plasma aldosterone and aldosterone secretion rates; proteinuria versus lack of blood pressure control; G6PD and abnormal haemoglobin status; comparison of Propranolol with angiotensin converting enzyme inhibitors like Captopril on blood pressure control; etc. But even without special funding there is still much that can be done in the field of African anthropogenetics by probing the readily accessible genetic effects of polygamy not only on hypertension as Dr Addy has done, but also on sickle cells and common African traits like hereditary deafness and left-handedness and its connection with hereditary stuttering. While the wealthy developed countries have, expectedly, produced most work in hypertension, the developing countries can, unexpectedly, make valuable contributions using mundane disciplines like clinical and genetic epidemiology.

"Hypertension research," say Edwards & Carey, "has been likened to the man who lost his car keys in a poorly lighted car park. A passing stranger offered to help and spent some minutes searching in vain before asking the hapless motorist 'Are you sure you lost your keys in this part of the car
park?" 'No', replied the man, 'I am not sure, but
the light is much brighter here' ".

Dr Addy seemed to have begun looking for the
keys right where he was, in the dark, and found
them!

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