EDITORIAL

A CASCADE OF BIOCHEMICAL AND PHYSIOLOGICAL MARKERS IN PATHOLOGICAL DISORDERS

A few years ago, a neurophysiology lecturer in the Department of Medical Physiology, University of Nairobi, was doing some research on possible indicators in malnourished children. The first indicator he chose was the electroencephalogram (EEG). Would this parameter be significantly different in malnourished as compared to well-fed healthy children? Out of curiosity, I sought the opinion of a paediatrician regarding possible outcome of this research. What I got was totally unexpected. The paediatrician went ballistic; with a furrowed brow, hissing and his hands in the air gesticulating spasmodically, he could hardly control his emotions. As far as he was concerned, the only answer the researcher would get would be "I am hungry, I am hungry, I am hungry, feed me!" Paediatricians are known to get emotional when the welfare of their patients is threatened but clearly the procedure of getting EEG is much less invasive than getting blood for diagnostic purposes. So what provoked the paediatrician? This could best be answered by posing a rhetorical question: "Why do we disapprove the use of pictures of malnourished African children and elderly people by religious missionaries and non-governmental organizations (NGOs) to solicit funds from foreign donors?"

I recalled this episode when editing an article in this issue of the journal. The article by Kwena *et al.* is on "Possible biochemical markers in protein-energy malnutrition and malaria in children in Western Kenya". I can only speculate on how the paediatrician referred to above would react if he was to read this article. I doubt that his reaction would be different. A popular theme in medical research is how one pathological condition impacts negatively on other organs and physiological systems and what markers can be used to monitor these cascading changes. For example, haemolysis of red blood cells (RBC) common in malaria can lead to many other changes. Potassium (K^+) content of RBC is about 100 mmol/litre while that of plasma is 4 mmol/litre. Haemolysis of RBC can increase the plasma K^+ to more than 40 mmol/litre. Yet we know that plasma K^+ of 10 mmol/litre can interfere with cardiac function. Fortunately, K^+ resulting from haemolysis of RBC is rapidly distributed into cells and excreted in kidney. It would have been interesting for Kwena *et al.* to see if they could detect any changes in the electrocardiogram (EGG) of the children infected with malaria.

Another example is the disorder of renal function (nephropathy), leading to peptic ulcers, uremia (chronic anaemia), and hypertension. What is the connection between compromised renal function and the above disorders? Decreased excretion of gastrin leading to its accumulation in plasma leads to increase in secretion of gastric acid (HCl) and ultimately to peptic ulcers. Similarly, increase in blood urea nitrogen (BUN) will accelerate the destruction of RBC, reducing the lifespan from 120 days to less than 80 days. Furthermore, the decreased erythropoietin synthesis (produced in the kidney) will mean reduced erythropoiesis thus reducing the number of RBC even more. The reduced urine output will trigger activation of renin-angiotensin system culminating in hypertension and tachycardia. Renin is synthesized and stored in the juxtaglomerular apparatus and its secretion is controlled by several factors, including the sympathetic nervous system. Released catecholamines lead to tachycardia.

Yet another example is hepatic disorders which have far reaching consequences than the renal disorders above. Decreased microsomal enzymes responsible for drug metabolism will lead to accumulation of drug in plasma because of decreased excretion. For drugs with low therapeutic index such as warfarin and digoxin, the consequence can have far reaching ramifications. Reduced plasma albumin and α_1-acid glycoprotein common in malnourished children will mean less protein-binding of drugs leading to high

plasma concentration. In one of the studies reported in literature, sulphonamides given to malnourished children at normal therapeutic doses were shown to be toxic because of reduced plasma proteins. In the more advanced cases of liver cirrhosis one can expect a cascade of biochemical and physiological markers which at times are difficult to interpret.

The above examples are given to show how a disorder such as malaria can lead to a multiplicity of changes and often the clinician may find it difficult to establish the correlation between a myriad of symptoms which appear to be totally unrelated.

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