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LETTER

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The metabolic syndrome, babies and bathwater

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There is a phrase in the English language that entreats the unwary not to 'throw the baby out with the bath water'. It means be careful not to jettison what's valuable when throwing out the rest. The Editor's polemic on the metabolic syndrome [1] may risk jettisoning a lot that is valuable.

The metabolic syndrome clearly exists. It is all around us. We see it every day, and health services spend a lot of money on managing it. Just because we find difficulty in defining it quantitatively does not deny its existence. Perhaps we would gain more from trying to understand why it eludes clear definition and adapting our practice accordingly.

Current understanding suggests that hyperinsulinaemia, associated mainly—but not exclusively—with obesity, drives a variety of apparently unconnected disturbances, including dyslipidaemia, hypertension, hyperviscosity, hypercoagulability, hyperuricaemia and (in the female) hyperandrogenaemia. The link between obesity and these disparate metabolic changes is insulin resistance, which weakens control of blood glucose. The rise in glucose feeds the hyperinsulinaemia.

So what are the difficulties with the definition of metabolic syndrome? Imagine insulin resistance as the hub of a cartwheel whose spokes each represent one of the disturbances it drives. This representation offers four important constructs. First, it is the hub alone that causes the wheel to turn. Second, the spokes are all connected to a single hub—when one moves on account of increasing insulin resistance, the others move as well—this is what makes insulin resistance a syndrome. Third, no single spoke causes movement in another—all are driven centrally. Dyslipidaemia (heart disease) is not caused by high blood glucose (diabetes). Dyslipidaemia is merely an association of hyperglycaemia, dependent like all the other spokes on power from the hub.

Fourth—and crucial to the issue of definition—is the individual response of each spoke to the driving force of insulin. Individual people might be expected to respond differently in this respect for genetic reasons. Accordingly, some individuals subject to hyperinsulinaemia may become severely dyslipidaemic before they become diabetic. Indeed, some may die of a coronary thrombosis before they become diabetic, though it should be remembered that around two-thirds of those suffering their first coronary are either glucose intolerant or (often unknown to them) diabetic. Others with diabetes may die of a hypertensive or thrombotic stroke before they suffer a heart attack (though all will show evidence of coronary disease at autopsy).

The inevitable variation in behaviour of the various spokes in different individuals does not invalidate the existence of a syndrome. It merely frustrates attempts to categorise it quantitatively in a way that applies to everybody. Mankind seeks neatness in classification, but why should nature respect such attempts at taxonomic elegance?

Metabolic syndrome is the multi-system expression of a single metabolic disturbance, namely, hyperinsulinaemia (with due recognition of the possibility that intermediaries such as adiponectin may play a key role). This is not the *reification* of an abstraction. The risk of cardiovascular mortality is clearly related to the combined length of each spoke of the metabolic wheel. Single spokes (e.g., lone hypercholesterolaemia) have little implication for heart disease.

But the real danger of throwing out the metabolic syndrome as mere myth is the loss of an opportunity to rationalise health services that would go with it. Miss IR may well be visiting the diabetes clinic on Monday, the hypertension clinic on Tuesday, the lipid clinic on Wednesday, the weight management clinic on Thursday and the infertility clinic on Friday. For purely historical reasons of clinical classification, patients make multiple visits to multiple clinics to see multiple nurses and multiple doctors who write multiple scripts for multiple

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drugs to treat the multiple end-stages of a single disturbance: insulin resistance. The waste in terms of duplication of structure and effort must be immense, and our new understanding of the metabolic syndrome invites us to organise our care pathways more logically.

The way forward is recognition of the syndrome as reality, and its translation into a single 'metabolic' clinic that treats insulin resistance as a single modifiable entity rather than struggling to contain its multiple outcomes as separate end-stage diseases. There is substantial evidence that insulin re-sensitisation can slow or even halt the metabolic wheel, and the cost-effectiveness of braking the hub may be substantial.

Reference

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