Seek not to find out who is biased. It could be you.

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1 Darwin NC. Journal of Research (1845).
4 Sackett DL. Bias in analytical research, Journal of Chronic Diseases 1979;32:51-63.

Misconceptions about blood lead concentrations

Physicians and students are taught that blood lead measurements should be used to diagnose lead poisoning. Once looked upon with uncertainty, this axiom is becoming increasingly adopted. Recently the National Institute for Occupational Safety and Health (NIOSH) has officially “defined (sic) lead poisoning as a concentration of lead in whole blood exceeding 50 μg/dl”. Such a definition and the whole concept of any “diagnostic blood lead concentration” have no scientific grounds but have instead involved two perplexing and challenging features: the stability of lead in the blood stream and the importance of the right timing of toxic lead action.

The first assumption compels us to question why an individual blood lead reading itself should imply an active current clinical state (poisoning). It could indicate nothing more than an immediate “cross sectional” concentration of lead at a particular point in time. All other possible implications are speculative extrapolations unsubstantiated by any evidence. Clinical experience has shown that “diagnostic” concentrations of lead in blood, whatever they may be, are often variable, transient, or at best floating within more or less wide limits and with no balance between input and output. This is quite comprehensible: the human body has no homeostatic mechanisms to maintain lead at any constant blood concentration against the prompt natural urge for clearance; animal physiology can barely succeed in safeguarding the indispensably constant blood concentrations of the essential metals let alone that of a foreign, useless, and harmful one. The persistence of a blood lead concentration would otherwise entirely disprove the evolutionary principles of selection and survival. Bearing this in mind it would be beyond sound medical reasoning to recommend an unstable, oscillating value of a chemical test as the reliable basis for a clinical diagnosis if this were the only sign in a symptomless person. The experts seem to agree: “Too much reliance must not be placed on the figures for blood lead” says Hunter; “It is not a precise index of adverse effect per se, even at elevated levels” warns Chisolm; “Its main value is to monitor abnormal exposure in a population rather than to serve as a major diagnostic tool” concludes Waldron. These opinions, however cautiously expressed, clearly suggest the diagnostic irrelevance of the blood lead concentration in clinical poisoning, the more so because the concentrations “return to normal even though exposure was excessive”.

Nevertheless, a “diagnostic” lead blood concentration has been taken as the basis for a nationwide plan to eradicate childhood lead poisoning in the United States and a “call for lowering of the definition (sic) of lead poisoning from a blood lead level of 25 μg/dl (1.20 mmol/l) to 10 μg/dl (0.050 mmol/l)”5. This still seems to be of concern as some authors have established a blood concentration of 0.016 μg/dl as the “natural” blood lead concentration and announced that there may be no threshold concentration for lead toxicity. “Preventive medicine’s latest goal” could be of course idealistically and enthusiastically ex officio proclaimed to be a zero lead blood concentration but only if we take all the lead out of the air and the diet or only after we change the geochemistry of our planet.

The second crucial source of error and misinterpretation is due to the failure to recognise the necessity of timing toxic lead action. An often quoted and a less cautiously expressed belief is that an increased blood lead value “reflects (only) a very recent or current exposure”6.7 Whereas this, of course, may be absolutely true, it may also have an alternate yet equivocal implication: the increased value may instead be a point in the natural decline of lead in the blood after a much higher, past episodic peak but with no present existing exposure. Lead in blood may thus become low and unremarkable after damage has been done8 and still persists clinically. To correlate this (recently) lowered or low blood lead with present, persisting symptoms and signs of past lead effects would clearly be patent nonsense. Incredibly enough, however, this is just what has been occurring repeatedly. In childhood neuropsychological deficits, brain damage supposedly due to neurotoxic action of lead in the most vulnerable phase of brain development, possibly even before birth, it is thought to be induced, if at all, by a peak exposure in the past long before the finding of a low blood lead. Nevertheless, in most studies it is inferred that this low level can have deleterious neurotoxic effects! If this were true, one wonders how mankind has managed still to exist. An even better example, devoid of the inevitable myriad of confounding variables in childhood neurobehavioural abnormalities, is the clinically manifest lead palsy in adults with undoubted evidence of lead exposure. In most patients, at the time of an existing overt palsy the blood lead concentrations were low (normal and acceptable). Moreover, the misinterpretation of a low blood lead concentration in lead induced slowing of motor nerve conduction velocity went so far as to recommend electroneurography as an early test of lead exposure ignoring the fact that the slowing, if present at all, is in lead poisoning rather than the sign of a spinal lesion,9 damage having taken place long before the present low blood lead finding. Similar in this regard is the laboratory finding of raised erythrocyte protoporphyrin as a sign of a delayed and long term effect of lead induced inhibition of mitochondrial erythroblastic ferro-chelates. It is well known, although inadequately appreciated, that this sign of lead action may persist long after exposure has ceased10 and the blood lead has returned to a normal low concentration. It is stated11 that in children the enzyme is inhibited at a blood concentration of about 15 μg/dl although there are opinions that the test is insensitive and not reliable at blood concentrations below 25 μg/dl.12 These
apparent controversies lead to the final question: why blame the sensitivity of the test instead of stating that in the symptomless person there is no toxic action of lead? In my long clinical experience I have never seen a normal protoporphyrin in any person with other reliable evidence of chronic lead toxicity.

Should we, in a symptomless person with suspected overexposure to organophosphate and with normal acetylcholinesterase activity, blame the test for the lack of sensitivity or simply infer that there is no poisoning?

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