There are three so-called laws that underlie the science of toxicology. Paracelsus is usually considered to be the father of toxicology, having formulated the first law, which states that the dose makes the poison. The second law concerns the specificity of toxic effects of individual chemicals, a specificity due to the unique chemical structure of the agent and the laws of biology that govern the response. The third law is that humans are animals and that therefore the study of animals can provide useful insight into effects in humans.

We can find no record of any eponym being used to designate the second law of toxicology. We propose that the place of honor for having clearly enunciated this second law, which encompasses recording an unfortunate experiment to prove his dictum, belongs to Paré, who stated that “Poyson . . . kills by a certaine speciﬁc antipathy contrary to our nature” (Paré, 1634/1951).

Paré (ca. 1510–1590) was born in the French city of Laval and grew up in humble circumstances that left him unable to attend the university (Gunn, 1941). After apprenticeship as a barber-surgeon, and three years performing surgery at the Hotel Dieu, a Paris public hospital, Paré began his long career as a military surgeon. His medical activities were typified by a practical approach to treating battlefield wounds, based upon careful observation and a willingness to challenge the doctrines of the Faculty of Medicine. Among his contributions were the reintroduction of the ligature to tie off bleeding blood vessels and the abandonment of boiling oil as a routine treatment of battlefield injuries. His published arguments for use of ligatures, an approach contrary to that advocated by medical academicians at the University of Paris, combined both ﬁeld experimentation and citation of ancient literature. His fame led to his providing medical advice to four successive French Kings, and such well known contemporaries as Catherine de Medici, Rabelais, and Montaigne (Gunn, 1941).

Paré makes his case concerning the specificity of poisons on a treatise on the Bezoar, reputed to be an antidote against all poisons (Paré, 1634/1951):

This stone is found in sundry shapes, but commonly it resembles an Acorne or Date-stone. . . . Now this stone is light, & not very hard, but so that it may easily be scraped, or rapsed like aalabaster; it will dissolve, being long macerated in water; at ﬁrst it was common amongst us, and of no very great price, because our people who trafﬁcked in Persia, bought it at an easier rate. But after that the faculties thereof were found out, it began to bee more rare and deare, and it was prohibited by an Edict from the King of the countrey, that no body should sell a Goate to the stranger Merchants, unless he first killed him, and tooke forth the stone, & brought it to the King.

. . . They use it . . . not onely against poysons, but also against the bites of venemous beasts. . . .

Some years agoe a certaine Gentleman, who had one of these stones which hee brought out of Spaine, bragged before King Charles then being at Clermont in Auverne, of the most certaine efficacie of this stone against all manner of poysons. Then the King asked of mee, whether there were any Antidote which was equally and in like maner prevalent against all poysons? I answered, that nature could not admit it; for neither have all poysons the like effects, neither doe they arise from one cause; for some worke from an occult and speciﬁc property of their whole nature, others from some elementary quality which is predominant . . . and that it was an easier matter to make triall hereof on such as were condemned to bee hanged. The motion pleased the king; there was a Cooke brought by the Jailor who was to have been hanged within a while after for stealing two silver dishes out of his masters house. Yet the King desired ﬁrst to know of him, whether hee would take the poison on this condition, that if the Antidote which was predicatated to have singular power against all manner of poisons, which should bee presently given him after the poison, should free him from death, that then he should have his life saved. The Cooke answered cheerfully, that he was willing to undergo the hazard. . . . Therefore he then had poyson given him by the Apothecarie that then waited, and presently after the poyson, some of the Bezahar brought from Spain, which being taken down, within a while after hee began to vomit, and to void much by stoole with grievous torments, and to cry out that his inward parts were burnt with ﬁre. Wherefore, being thirsty, and desiring water, they gave it him; an he after, with the good leave of the Jaylor, I was admitted to him; I ﬁnd him on the ground going like a beast upon hands and feet, with his tongue thrust forth of his mouth, his eyes fierie, vomiting, with store of cold sweats, and lastly, the bloud ﬂowing forth by his eares, nose, mouth, fundament and yard. I gave him eight ounces of oile to drinke, but it did him no good, for it came too late. Wherefore at length hee died with great torment and exclamations, the seventh houre from the time that hee tooke the poison being scarcely passed. I opened his body in the presence of the Jailor and foure others, and I found the bottome of his stomacke blacke and dry, as if it has beene burnt with a
Cautery; whereby I understood he had sublimate given him; whose force the Spanish Bezahar could not represse, wherefore the King commanded to burne it. (emphasis added)

We of course would not countenance experimentation on prisoners for very many good reasons, although perhaps even the most knowledgeable toxicologist would have made the same choice as did the cook.

Paré similarly debunked the reputed value of the unicorn’s horn as an antidote against all poisons, making for its time the shocking statement that unicorns did not exist, and even if they did the horns would have no value (Gunn, 1941). Paré’s writings, with his rigorous approach to determining what works rather than simply accepting the dictates of the past, form the basis for experimental surgery. He was attacked by leading academics on a variety of grounds, not the least of which was that he was not trained in Latin and therefore wrote in French. His retort was that Hippocrates also wrote in his native language (Keynes, 1951).

This would be a valuable time to reaffirm the importance of the second law of toxicology. It is under attack from many quarters, including from those who would label all chemicals as having the same hazard. While this at times may be the easy regulatory solution, it is not the right solution, nor is it one that leads to developing the best use of toxicological science.

Careful attention to Paré’s law would preclude our treating every chemical as if it is a carcinogen. It might also prevent some of the more egregious toxic tort lawsuits, such as the one alleging that nitrobenzene causes leukemia because it has a benzene ring, or that toluene causes allergic asthma because toluene disocyanate is capable of doing so.

Paracelsus (1493–1541), a somewhat older contemporary, shared a number of viewpoints in common with Paré. They both emphasized the value of practical experience and were disdainful of longstanding theories handed down in books or by the Academy. Paracelsus made special note of the value of learning from military medical practice, an approach that foreshadowed the major advances made by Paré. Paracelsus was arguably the more broadly traveled and inquisitive of the two, delving into medical and social conditions throughout the European continent and into many contemporary approaches, including magic and alchemy. His voluminous writings are on a wide range of topics, including forays into the social context of health and of medical practice that recently served as the basis for a major symposium exploring the relevance of Paracelsus to modern health policy (Mercurio and Backhaus, 1995).

Honoring Paré has the advantage of adding truly a great man to our history, one in whom we can take unqualified pride. Paracelsus certainly deserves respect for his scientific activities and insights, which led to formulation of the first law of toxicology. Unfortunately, Paracelsus was also an alchemist and at least a bit of a charlatan, and a fraud in his public activities. In contrast, Paré was an authentic hero of his time, greatly respected for his scientific skills and for his life saving care of the common soldier.

REFERENCES


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