myocardium, which might also be useful for improving the control of digitalis therapy.

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EDITORIAL
How Magic Is the Bullet, and What Will It Do?

In their article on the selection and testing of ouabain analogs for cardiac imaging, Fujibayashi and his colleagues have re-opened for us a chapter in one of the earlier books in nuclear medicine: radiopharmacy. First, their exploration of analogs had embedded two challenges: which bullet is most magic in seeking out the myocardium in preference to other sites, with special attention to other nearby sites; which could interfere with image interpretation? And which bullet will carry a strange—a biologically foreign—gamma-emitting element (preferably iodine or technetium) to the target? The chemistry imposes two demands: to find the magic carrier and to devise a bond sufficiently attractive to remain attached to the carrier for several hours, while under the influence of the body’s fluids, without so altering the handling of the compound that it might lose some of its magic.

Phase one of the search used the biologically perfect master spy, ³H, which allows the candidate bullet to be tested for its magical qualities: How well will it seek the target when it has to carry no (biologically) sinister gamma-emitting baggage? Compounds A and B passed the test. (Perhaps the radiopharmacists in Dr. Fujibayashi’s group added to their store of knowledge about the nature of the interaction between ouabain, its biochemical close cousins, and the myocardial membrane in the process of looking at these data. Why A and B, and not C and D?)

In phase two, selection of the gamma-carrying element, has meant “try iodine first” in the “before technetium” decades, and then “we should consider technetium” in the subsequent history of radiopharmacy. The radiochemical triumph of taming ¹²³I among its lesser imaging-friendly cousins is a legacy to subsequent generations. Tracer iodine is more expensive and less available than tracer technetium, but the art of modern radiopharmacy delivery services, at least in big cities, addresses this issue.

Phase three, the first to engage the nuclear medicine department with its imaging equipment, requires the choice of a surrogate for man, the animal model. Some care is required: a small kinship of myocardial tracers.
recently explored worked well in dogs, but not in humans, in a slightly earlier saga on the way to sestamibi and teboroxime (1). If phase three is successful (ouabain has made it this far with this publication), phase four will match it up to the existing arsenal of radio-bullets, thallium, sestamibi, teboroxime, and perhaps others that are under development, to discover a possible advantage.

The critical tests, the myocardium/blood, myocardium/liver, and myocardium/lung ratios are competitive (2,3). The tracer will go on to the bedside via pathways that are well known to pharmaceutical houses. Will it compete with existing myocardial imaging agents?

Or is there another benefit algorithm? What can we learn from the saturation kinetics shown in Figure 3? Should we, like early nuclear medicine pioneers, be more interested in this tracer for its functional imaging potential, the localization and quantitation of Na-K ATPase? Will ouabain offer the cardiologist a new tool, the semiquantitative analysis of a myocardial enzyme, either as a measurement of the patient’s capacity to respond to higher doses of digoxin, or as a predictor of a myocardial metabolic reserve?

Could a three-dimensional cardiac ouabain map be registered in computer memory and compared with a thallium or sestamibi map, done before or after, providing a regional measurement of enzyme distribution? Would a rest-exercise ouabain map disclose metabolic distress, or stunned myocardium, with greater interpretive benefit than the comparable ischemic distress imaged with now popular perfusion agents?

Fujibayashi shows remarkable speculative reticence by giving just the bare bones of what has been accomplished, with the single clinical suggestion that digoxin therapy might be guided by such imaging. I believe that it would be the rare patient whose need for fine-tuned digoxin requirements would be sufficiently critical to justify serial imaging to make a dosing decision. However, the invention of an in vivo, three-dimensional map for any enzyme system is news. We are invited to consider a family, or perhaps a larger kinship, of potential research and clinical derivatives of this new magic bullet and its potential applications.

In this paper, we are reminded of our dependence on our chemist and pharmacologist colleagues for pointing to new opportunities. And we are in parallel reminded of the obligation of the complete clinician to sort out the physiological and clinical applications of such opportunities as may bring benefit to our patients and our research.

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