Perspective on the Historical Note on EIA/ELISA by Dr. R.M. Lequin

I am pleased and humbled to see Dr. Lequin write about my work on ELISA in his historical note (1). Unfortunately, my thesis advisor, mentor, and friend, Peter Perlmann, cannot read it, as he recently passed away. One summer day 35 years ago, I knocked on the door of Professor Perlmann’s office at Stockholm University to ask him if I could be a graduate student in his department. He accepted me into his laboratory, and we agreed that I would try to develop an immunoassay based on enzymatic readout. After talking it over with Peter and reading the literature, I combined the format of RIA (2), enzyme labeling of antibodies (3), and the coating of plastic with proteins (4) in my experiments. From the very beginning, I referred to the assay I was trying to develop as ELISA, and that acronym stuck. We were convinced that enzyme immunoassays (EIAs) were going to be the future of immunoassays and were happily unaware of the previous skepticism mentioned in Dr. Lequin’s article. I vividly remember when, on a cold winter day in early 1970, I had the first successful ELISA result.

We never thought of patenting our invention. Fortunately, the Organon patent on EIA did not cause too much of a delay in the acceptance and use of ELIA and ELISA. The patent situation may have made companies hesitate to get into the technology, but it did not deter researchers in academia. I was particularly pleased when already in the early 1980s ELISA became an accepted abbreviation that required no explanation in the Journal of Cell Biology.

Dr. Lequin emphasizes the development of automation of ELISA/EIA as an important factor in the widespread use of these assays in clinical laboratories today (1). However, to me, it was clear from the very beginning that ELISA might have its greatest impact in areas where RIAs and other more technically complex assays would never have been used. You could not possibly envision a home pregnancy test carried out in the form of an RIA! So when Dr. Alister Voller suggested that we try the ELISA for malaria field diagnostics in East Africa (5), I was all in favor of testing the robustness of our assay under the most challenging conditions of the African bush. On a 1-month field trip to Tanzania, we collected and tested blood samples for the presence of malaria antibodies, using microtiter plates and a portable spectrophotometer as our only instrumentation. This field trial was a success. We did not know at that time (in 1975) that HIV was endemic in the area where we bled hundreds of people without using any special protection, but luckily nothing bad happened. And now, one of the main applications of ELISA is the screening test for HIV.

Dr. Lequin stresses the impact that ELISA/EIA has had on human medicine (1), but one should not overlook the impact these assays have had, and continue to have, in experimental research, veterinary medicine, and agriculture. I for one have used various improvised ELISAs throughout my entire research career, and so have most of the people I know in science. It has been very helpful that companies have manufactured numerous enzyme conjugates, mostly antibodies, that can be used together with microtiter plates to devise very simple, sensitive, and flexible assays. In addition, I was delighted to be consulted already in the early 1980s by researchers who wanted to apply ELISA to such varied and exotic tests as viral diseases of poinsettias and bacterial diseases of dolphins. Although the number of publications in agricultural fields may be lower than in human medical fields, the economic impact is quite significant. Nearly every assay in a veterinary diagnostic laboratory is an ELISA. Recently, I wanted to breed one of my dogs and had her tested for serum progesterone to determine the time of ovulation. The test was performed in a rather primitive laboratory and could detect progesterone at concentrations of a few nanograms per milliliter, and it was completed in ~1.5 h. I was very impressed with the sensitivity, accuracy, and speed of that ELISA. And the dog was successfully bred.

Most recently, an article in the Los Angeles Times reported on the use of ELISA in the determination of the nature of the original coating of a famous piece of artwork (6). There seems to be no limit to the uses to which ELISA can be put!

Dr. Lequin ends his article (1) with the inventors of ELISA/EIA deserving to be honored. I have received many honors, but the real honor is to know that what we did 35 years ago is still useful in medicine and other fields.

References
6. Muchnic S. A cabinet, an egg, and an antibody; one crucial detail of a masterpiece seemed off, but what did the maker intend? How biologists helped unravel an art-world mystery. Los Angeles Times 2005;September 4:E34.

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