

COMMENTARY

By Bernard Dixon

A LESSON FROM LOUIS PASTEUR ON AIDS VACCINE



A non-medically qualified individual uses material of unknown composition and toxicity to treat patients, including a child, who may be suffering from a potentially fatal illness. The individual does not even try to obtain informed consent, but publishes patients' names and addresses to help publicize some astounding claims. Moreover, like fraudulent quacks the world over, the individual

keeps details of the "treatment" secret, so that its validity cannot be independently validated. Perhaps worst of all, this reckless person injects human beings with an extremely virulent micro-organism before conducting tests in animals. Some patients die, and a close collaborator who is a medical doctor dissociates himself from his colleague's work.

The biotechnologist who took these risks, yet emerged with thunderous acclaim for his astonishing triumph in defeating rabies, was Louis Pasteur. He came vividly to mind several times during *Nature's* recent London conference on "New Technology in Biotechnology". Two of those moments are pertinent in suggesting that the wholly desirable swing toward greater safety in biomedical innovation that has occurred over the past century may have gone much too far.

First, there was the discussion after a paper in which Professor Luc Montagnier from the Institut Pasteur in Paris had described the possible value of recombinant and synthetic peptides to immunise susceptible people against AIDS. Despite ideas such as the use of thymosin as a vaccine, reported recently by Allan Goldstein and colleagues (*Science* 232:1135, 1986), all agreed that the prospects for early practical help were not good. Yet the horror grows apace, the thousands of victims in the U.S.A. and Europe now being overshadowed by the likelihood of a plague of unthinkable proportions in East and Central Africa.

Why then, asked the distinguished immunologist Avron Mitchison, has inactivated HTLV-III virus not been tried already as a vaccine, in small-scale, exploratory trials? "Does not some of the blame attach to the lawyers and legislators who have overmuch grip on our society?" Professor Mitchison continued, answering his own question. One obvious analogy, he said, was with yellow fever, which had been combatted by immunization well before much was known about its causative virus.

Later the same day, we heard from Tom Lehner of Guys Hospital, London, about the use of monoclonal antibodies against *Streptococcus mutans* to thwart the development of dental caries. First with primates and more recently with human subjects, Professor Lehner has shown that regular application of monoclonals to teeth impairs colonization by the bacterium and thereby reduces caries to almost zero. It seems that the antibodies prevent *S. mutans* from adhering to salivary glycoprotein on the teeth, rendering them vulnerable to opsonization

and phagocytosis by the local traffic of neutrophils.

Given the continued burden of dental decay, this is excellent news. Significantly, however, it represents Professor Lehner's *second* successful research project designed to harness streptococcal antibodies in the battle against caries. The first, based on *active* immunization, ended four years ago after Lehner began to realize that regulatory approval would probably never be forthcoming for a parenteral prophylactic against a condition which is scarcely life-threatening.

It's instructive to contrast these modern realities with those of Pasteur. As well as living in a different age, the pioneer biotechnologist did of course enjoy inspirational good fortune. As Gerald Geison has suggested in the *Hastings Center Report* (8:2, 26, 1978), Pasteur violated several ethical and scientific precepts in his work. He started to give little Joseph Meister "aged" spinal marrow, thought to carry attenuated rabies virus, a month before he tested the same material in animals with the disease. Success in those experiments was only "partial". And Pasteur could not even be sure that his spinal cord tissue actually contained rabies virus. What he did suspect was that at the end of his series of inoculations with increasingly virulent potions, the boy was receiving material even more dangerous than that obtained from rabid dogs. Yet he had previously refused to treat a bitten child, insisting that "proofs must be multiplied *ad infinitum* on diverse animal species before human therapeutics should dare to try this mode of prophylaxis on man himself."

Dr. Geison argues that there were mitigating circumstances. Rabies had long been considered an especially wretched disease, its victims often being reduced to total physical and mental degradation as quivering, animal-like shadows of their former selves. Long before Pasteur, the fear of rabies was sufficient to make people submit voluntarily to virtually any plausible therapy, even one as excruciating as cauterization by fire or acid.

More telling to modern eyes is the criticism that Pasteur's vaccine, unlike that of Edward Jenner, was contrived in the laboratory. In 1796 Jenner, too, had done something which now seems questionable. He inoculated cowpox matter into the arm of a *healthy* lad, James Phipps, and gave him smallpox pus six weeks later. But the cowpox matter did come from nature, and Jenner's confidence was founded on ample observations on the natural relationship between the two infections. Pasteur's approach was quite different. There was a real prospect that, by manipulating his presumed rabies virus in the laboratory, he could have created a novel, artificial form of the disease.

It's worth considering the parallels with AIDS today. This disease, too, is wretched and potentially fatal. Yet we are waiting upon highly sophisticated laboratory manipulations as a possible source of vaccine, while ignoring the natural virus, killed according to the principles first enunciated by Louis Pasteur. Is this wise? After all, those principles *are* now very well attested indeed.

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