

It has been said that Dr. Dienes had three careers, one in cellular immunity, a second in mycoplasma research, and a third as an artist.

I would like to remember with you today a period in the early working years of Dr. Dienes, a period that is not generally remembered by the public and is even forgotten by many of his research colleagues. This early period or first career was devoted to the study of an important type of immunity occurring in man and animals that is generally referred to as delayed hypersensitivity or tuberculin hypersensitivity or cellular immunity.

Dr. Dienes came to this country from his native Hungary in 1922 and initially worked at a Tuberculosis Sanatorium in Ashville, North Carolina. There, in the von Ruck Research Laboratory for Tuberculosis he initiated a classic series of studies on immunity which were to take more than 15 years to complete both in Ashville and subsequently at the Massachusetts General Hospital in Boston. This was a time when immunology was in its infancy and when the term immunity generally referred to humoral community; that is, to the development in the blood of antibodies. However, it was also becoming clear at about this time that there was another form of immune response, which protected organisms against certain bacteria such as tubercle bacilli. This form of immunity, DH, apparently did not involve circulating antibodies and was mediated by sensitized cells, lymphocytes. Hans Zinsser, who was at that time Professor of Bacteriology at HMS, was himself interested in this area and had in fact coined the term DH. He was instrumental in recruiting Dr. Dienes from Ashville to the MGH.

As we now know, DH is probably the hosts' prime means of resistance to a variety of bacteria (such as Tbc), many viruses (from small pox to measles), malignant tumors, and its expression is also an important medical problem in that it is responsible for rejection of heart and kidney transplant. It is

also something of a nuisance, being responsible for such petty annoyances of every day life as poison ivy. Dienes, along with Zinsser and a very few others was the first to recognize this response, to distinguish it from the already well known antibody-mediated reactions, and to define its properties. His work provided the solid foundation on which all subsequent work was based.

To be more specific Dienes made three fundamental discoveries during the 15 year period he devoted to the study of cellular immunity.

The first was the first accurate description of the histology of delayed hypersensitivity reactions and their evolution. His studies clearly demonstrated that the tuberculin reaction and similar delayed type reactions consisted of perivascular mononuclear cell infiltrates which extended throughout the zone of skin test. They thus differed sharply from other types of inflammation in which neutrophils appeared first and were only subsequently followed by chronic inflammatory cells. On the one hand these findings set delayed reactions apart as a special type of inflammation and on the other distinguished this form of immunity from those mediated by antibody, such as anaphylaxis, which had an entirely different histology.

Unfortunately for the progress of science and medicine, these findings were not accepted immediately and universally. In part this reflected the fact that the times were not ready for Dr. Dienes' ideas and partly that other less careful investigators were unable to duplicate all aspects of the work. Now, however, some 45 years later, there is nearly unanimous agreement that Dienes was right and it is gratifying to know that Dienes lived to find his early work substantiated and accepted.

Dienes' second important discovery was the finding that delayed-type hypersensitivity could be elicited with non-bacterial antigens. This was a new and fundamental concept and indicated that the delayed response of

the host to foreign bacterial invaders was not unique but could be duplicated by non-living, highly purified antigens such as egg albumin. These observations greatly facilitated the study of delayed hypersensitivity which had been hindered by the requirement for studies with living and often virulent organisms. It also prepared immunologists for the subsequent recognition that delayed hypersensitivity was the single most important mechanism in resistance to many tumors and viruses and was crucial in the rejection of foreign grafts of tissue.

Dienes' third important discovery was the finding that delayed hypersensitivity could be initiated in the absence of infection or contact with tubercle bacilli. Prior to Dienes' work it was widely believed that active infection with tubercle bacilli or other bacteria was required to initiate the delayed type of immune response. In fact, Dienes himself held this view initially and had discovered that the best immune response to purified proteins or other antigens was obtained when these were injected into sites of active tubercle infection. Guided by this observation, another investigator and co-worker of Dienes, Jules Freund, showed that killed tubercle bacilli, injected along with antigen in the form of a water and oil emulsion (complete Freund's adjuvant), greatly facilitated development of delayed hypersensitivity.

But Dienes' experiments were carefully controlled and he found that animals sensitized with protein antigens in the absence of tuberculosis infection also developed a form of cell-mediated hypersensitivity. This observation was forgotten for a time but has been rediscovered and is now recognized as a distinct and important form of cell-mediated hypersensitivity. It bears the unfortunate name Jones-Mote reaction but there is a movement afoot to rename it in Dienes' memory. After all, he discovered it.

It was a sad loss for immunology when Dr. Dienes changed his career interests in the late 1930's away from cellular immunity to studies of mycoplasma. A sad loss for immunology but an important gain for mycoplasma research. The reasons for this change in career direction were complex and were related to lack of available research funds. How external events do control us all.

Dr. Dienes was a great scientist and a quiet and unassuming man. His work was always careful and could always be repeated by careful investigators. Perhaps this is the finest thing one can say about a fellow scientist. It is clear that Dr. Dienes' memory would have lived even if he had not gone on to have a second career with mycoplasma.

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*for
Memorial Service
March '74*