

Addendum to Citizen's Petition Docket # 02P-0349/CP 1 filed on August 5, 2002, and addendum sent September 3rd

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Dockets Management Branch
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Department of Health and Human Services
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I have enclosed some additional information for the FDA to consider when reviewing Citizen's Petition Docket # 02P-0349/CP 1, filed on August 5, 2002, and an addendum submitted September 3.

I have additional regarding the mechanism of vaccine induced diabetes:

Additional information

Mechanisms by which vaccines have been proven to cause autoimmune diseases including diabetes has been extensively reviewed recently (1). In this paper the role of macrophages in causing IDDM was reviewed as referenced below. Data published since the release of this paper was written further supports the role of macrophages in the development of IDDM and explains why many vaccines will cause diabetes in a measurable number of recipients. The new findings indicate pancreatic islet cells naturally secrete chemotactic factors which attract macrophages. These latest findings explain an observation by Goto (2). Goto et al. described experiments showing that injections of guinea pigs with several different vaccines containing aluminum adjuvant caused inflammation in the pancreas (2). The amount of inflammation in the pancreas correlated with inflammation at the injection site.

Pancreatic islet cells are now known to secrete a number of chemotactic factors for macrophage (3-7). It appears that some of the chemotactic factors have secondary biological

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functions and are actually involved in controlling insulin release (7). Release of some of these chemotactic factors have been shown to be associated with the destruction of human pancreatic islet cells in islet cell transplants (6) and early onset diabetes (4). The production of the chemotactic factors by the islet cells also explains why vaccines, which activates macrophages, would be expected to destroy islet cells. The macrophages, activated by vaccines, circulate in the blood and are induced to migrate to the islet cells, by the chemotactic factors, where they kill islet cells and induce autoimmunity.

The following excerpt has been taken from a review on the mechanisms of vaccine induced IDDM (1).

"Type I diabetics have increased macrophage activity. It is believed that this increased activity precedes the development of IDDM and contributes to the onset of IDDM. Data supporting a causal relationship between macrophage activation and IDDM includes data showing humans at risk for IDDM because of family history have been found to have increased macrophage activity similar to that seen in diabetics (8,9). Animal models indicate that macrophages are involved in the initiation of diabetes (10) Many vaccines activate macrophages and would be expected to increase the risk of IDDM. Vaccines can both directly activate macrophages and indirectly activate macrophages through the release of cytokines. Macrophages are particularly stimulated by vaccine adjuvants including aluminum (11) and complex polysaccharides (12) similar to what are found in certain capsular vaccines like pneumococcal and hemophilus vaccines. Insoluble polysaccharides (12) like those found in vaccines are also more potent activators of macrophages than soluble polysaccharides which may be more common with natural infections.

Macrophages may increase destruction of islet cells by releasing cytotoxic molecules (13,14). Certain macrophages may preferentially increase the replication of Th1 lymphocytes (15) leading to destruction of pancreatic islet cells. Macrophages can injure pancreatic islet cells through the release of free radicals, nitric oxide, and cytokines including IL-1 and TNF (13). Activated macrophages also release alpha interferon. Alpha interferon has been repeatedly reported to cause IDDM in humans (16-19).

Activated macrophages can increase autoimmunity by presenting self antigens to autoreactive lymphocytes and activating the autoreactive lymphocytes. These autoreactive lymphocytes can kill islets through direct contact with the cells or through the production of soluble autoantibodies which destroy islet cells. The mechanism for inducing autoimmunity appears to involve a lymphokine drive phenomenon where the vaccine activates the immune systems and an immune response develops to autoantigens that are attached to MHC molecules on the same or adjacent antigen presenting cells as the vaccine toxoids. This phenomenon appears to occur in the draining lymph nodes (20,21) and is likely to involve both the direct

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*activation of macrophages (11) , the release of lymphokines capable of inducing autoimmunity
(22) and the up regulation of lymphokine receptors on cells (23)."*

Sincerely,

A handwritten signature in black ink, appearing to read "Bart Classen". The signature is fluid and cursive, with a long horizontal stroke extending to the right.

Bart Classen

Reference

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