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This Week's Citation Classic™

Peterson R D A, Kelly W D & Good R A. Ataxia-telangiectasia: its association with a defective thymus, immunological-deficiency disease, and malignancy. *Lancet* 1:1189-93, 1964.
[Pediatric Research Laboratories of the Variety Club Heart Hospital and Dept. Surgery, Univ. Minnesota, Minneapolis, MN]

Patients with ataxia-telangiectasia were frequently discovered to have an immune deficiency, a developmental defect of the thymus, a lymphoreticular malignancy, or all three. This paper documented this association and attempted to relate the clinical observations to the contemporary experimental work. [The *SCI*® indicates that this paper has been cited in over 270 publications since 1964.]

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Twenty years ago, our Minnesota group was aggressively evaluating every patient with an immune deficiency as part of a clinical and experimental study to elucidate the phylogeny and ontogeny of the immune system. Clinical experience often provided valuable insights that would influence experimental studies in the laboratory. The discovery of the tetrad of ataxia-telangiectasia, immune deficiency, thymic abnormality, and lymphoreticular malignancy served to reinforce our conviction that the thymus was central to the development of both normal and malignant lymphocytes.

The concept that a developmentally defective thymus might underlie disorders as disparate as immunodeficiency, lymphocytic malignancy, and autoimmune diseases was formulated and experimental studies initiated. This clinical experience thus facilitated the studies that led to our description of the two major developmental pathways of lymphocytes,[1] the pathogenesis of immunodeficiency diseases,[2] the realization that lymphocytic malignancies involve either T or B cells but not both, and can be so classified,[3] the demonstration of autoimmunity in thymectomized animals,[4] and the discovery that an oncogenic retrovirus can cause an immunodeficiency.[5] All of these observations have been dramatically expanded by investigators over the ensuing years and together constitute the substance of contemporary immunology. For example, the observation regarding the retrovirus-induced immunodeficiency anticipated the very recent discovery that a human retrovirus causes AIDS.[6] We suspect that the paper has been cited so often because it served to tie together these many clinical and biological phenomena.

A few words are especially in order about the human side of the story of ataxia-telangiectasia. The patient described as Case 1 would not have been discovered had not a colleague, Michael Blaw, told us she had ataxia-telangiectasia. He knew neurology, we knew immunology, but only the two of us could put the story together. A more poignant note concerns this patient and her family. It exemplifies the contribution these people make to medical knowledge, often at no benefit to themselves, and even to their further suffering. The family lived in North Dakota and the long drive to Minneapolis was hard for all of them. After almost two years of repeat visits and numerous immunologic studies, the little girl died one night in her home. Because the family knew of our intense interest, the father put his daughter in his car and drove her the hundreds of miles to Minneapolis so that we might perform an autopsy. That was the autopsy that confirmed the diagnosis of lymphosarcoma.

Very recently, I was consulted by the family of a girl with a progressive nervous system disease. She had ataxia-telangiectasia. I had to tell the family that we know nothing about the fundamental problem underlying this disease and thus had nothing to offer other than supportive services. The disease has done much for those of us interested in immunology; we have as yet to do anything about the disease.

R.A. Good is now professor of pediatrics at the University of South Florida, Saint Petersburg. W.D. Kelly is clinical professor of surgery at the University of Minnesota, Minneapolis.

1. **Cooper M D, Peterson R D A, South M A & Good R A.** The functions of the thymus system and the bursa system in the chicken. *J. Exp. Med.* 123:75-102, 1966. (Cited 605 times.)
2. **Peterson R D A, Cooper M D & Good R A.** The pathogenesis of immunologic deficiency diseases. *Amer. J. Med.* 38:579-604, 1965. [See also: **Peterson R D A.** Citation Classic. *Current Contents* (51):9, 18 December 1978.]
3. **Cooper M D, Peterson R D A, Gabrielsen A E & Good R A.** Lymphoid malignancy and development, differentiation, and function of the lymphoreticular system. *Cancer Res.* 26:1165-9, 1966. (Cited 30 times.)
4. **Sutherland D E R, Archer O K, Peterson R D A, Eckert E & Good R A.** Development of "autoimmune processes" in rabbits after neonatal removal of central lymphoid tissue. *Lancet* 1:130-3, 1965. (Cited 90 times.)
5. **Peterson R D A, Hendrickson R & Good R A.** Reduced antibody forming capacity during the incubation period of passage A leukemia in C_3H mice. *Proc. Soc. Exp. Biol. Med.* 114:517-20, 1963. (Cited 125 times.)
6. **Gallo R C, Salahuddin S Z, Popovic M, Shearer G M, Kaplan M, Haynes B F, Palker T J, Redfield R, Oleske J, Safai B, White G, Foster P & Markham P D.** Frequent detection and isolation of cytopathic retroviruses (HTLV-III) from patients with AIDS and at risk for AIDS. *Science* 224:500-3, 1984.