Selective IgA deficiency in chickens with spontaneous autoimmune thyroiditis

SELECTIVE IgA deficiency is believed to be the commonest form of human immunodeficiency disease, and occurs with a frequency of between 1: 500 and 1: 700 in random populations[1,2]. Although the isolated deficiency is often considered non-pathological, there is clinical and laboratory evidence that IgA-deficient individuals suffer more sinopulmonary infection and autoimmune and gastrointestinal disorders[3,4]. Family studies have suggested a genetic factor but no defined inheritance patterns have been established[4,5]. The chicken model has been used for a number of years in our laboratory to study the ontogeny of immunoglobulin class development[6]. Surgical bursectomy at hatching[7,8], treatment of chick embryos with specific antisera[7,9–11] and combined neonatal bursectomy–thymectomy[12] can result in depressed levels of IgA. This report describes recent observations of a selective IgA-deficiency that spontaneously occurs in the Obese strain (OS) of White Leghorn chickens. The OS chickens develop spontaneous autoimmune thyroiditis (SAT) at several weeks of age[13]. Clinical hypothyroidism is observed and high titres of circulating as well as bound anti-thyroglobulin antibodies can be detected[14]. The OS chickens were initially derived from the Cornell C-strain which reveals a 1% incidence of SAT. Selective breeding of CS birds, which showed phenotypic symptoms of hypothyroidism, resulted in the OS of which now, in generations 16 and 17, show 96% SAT. The histological and serological features in OS chickens make it a reasonable animal model to study Hashimoto's thyroiditis, an autoimmune disorder in humans[15].

Serum immunoglobulins IgY (ref. 16), IgM, and IgA were quantified by radial immunodiffusion in Agarose gel with heavy chain-specific antisera and reference standards prepared in our laboratory[17]. This technique is conventionally used to diagnose selective IgA deficiency in humans[18]. Both systems can detect IgA concentrations as low as 2–3 mg %.

In Table 1 the serum immunoglobulin concentrations of a random population of 6-week and 1-yr-old OS and CS chickens are presented. Serum IgA concentrations were markedly decreased in OS chickens with a mean concentration of 5.6 mg % in 6-week-old birds and 16.5 mg % in 1-yr-old birds. Although many of these OS birds had normal levels of IgA, 33% (4 of 12) 6-week-old birds and 16% (5 of 30) 1-yr-old birds had undetectable levels of IgA (<3.0 mg %). In contrast, only one CS bird had an IgA level of less than 10 mg % and none had undetectable levels of IgA. In addition to the isolated IgA deficiency in OS chickens, an increase in serum IgM levels were noted. It was observed, however, that the IgA-deficient birds did not necessarily have a selective increase in IgM, but rather the increased IgM was present throughout the entire OS population. This is consistent with the increased number of IgM-bearing B-cells found in OS chickens[19]. It has previously been reported that selective IgA deficiency in humans is often associated with increased amounts of serum IgM as well as increased number of plasma cells containing IgM in the laminia propria of the small intestine, indicating that a compensatory mechanism may occur in some individuals[3].

The relationship of autoimmune disease in humans to selective IgA deficiency has not been determined. While the majority of patients with autoimmune disorders have normal levels of IgA, those patients with the IgA deficiency have an increased incidence of abnormal κ/λ ratio, elevated levels of IgG and/or IgM, and serum 7S IgM[4]. Furthermore, those individuals who lack IgA have normal or increased numbers of IgA-bearing lymphocytes in the peripheral blood[20]. These observations suggest that the abnormality in the immune response occurs in the latter stages of cell maturation and results in the absence of IgA-secreting plasma cells. With the advent of an animal model for spontaneous IgA deficiency it is now possible to study the genetic and cellular events responsible for this deficiency. Indeed, preliminary experiments in our laboratory have already suggested a genetic relationship between IgA deficiency and alleles at the major histocompatibility locus in chickens.

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Table 1 Serum immunoglobulin concentrations in OS and CS chickens*

Line	Age	Number tested	IgY(mg %)† ±s.d.	IgM(mg %) ±s.d.	IgA(mg %) ±s.d.	Number with undetectable IgA	Total number with <10 mg % IgA
OS	6 weeks	12	228±2.9	146±1.3	5.57±3.9	4	7
CS	6 weeks	18	254±2.0	93.4±1.3	24.5±1.3	0	0
OS	1 yr	30	456±1.7	201±1.5	16.5±4.4	5	8
CS	1 yr	24	599±1.3	89.3±2.2	27.6±2.1	0	1

*Minimum sensitivity of the radial immunodiffusion assay is 2.0 mg % for IgY and 3.0 mg % for IgM and IgA.
†Serum immunoglobulin levels are presented as geometric mean. Analyses were performed on $\log_{10}$ transformed data.

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1 Bachmann, R., *Scand. J. clin. lab. Invest.*, **17**, 316–320 (1965).
2 Hobbs, J. R., *Lancet*, **i**, 110–114 (1968).
3 Ammann, A. J., and Hong, R., *Medicine*, **50**, 223–236 (1971).
4 Horowitz, S., and Hong, R., in *Immunodeficiency in Man and Animals*, **11** (edit. by Bergsma, D.), 129–133 (Sinauer Associates, Massachusetts, 1975).
5 Grundbacher, F. J., *J. med. Genet.*, **9**, 344–347 (1972).
6 Leslie, G. A., *Am. J. Vet. Res.*, **36**, 482–485 (1975).
7 Kincade, P. W., and Cooper, M. D., *Science*, **179**, 398 (1973).
8 Martin, L. N., and Leslie, G. A., *Proc. Soc. exp. Biol. Med.*, **143**, 241–243 (1973).
9 Martin, L. N., and Leslie, G. A., *J. Immun.*, **113**, 120–126 (1974).
10 Leslie, G. A., and Martin, L. N., *Int. Arch. Allergy*, **46**, 834–841 (1974).
11 Leslie, G. A., Stankus, R. P., and Martin, L. N., *Int. Arch. Allergy*, **51**, 175–185 (1976).
12 Perey, D. Y. E., and Bienenstock, J., *J. Immun.*, **111**, 633–637 (1973).
13 Witebsky, E., Kite, J. H., Wick, G., and Cole, R. K., *J. Immun.*, **103**, 708–715 (1969).
14 Cole, R. K., *Genetics*, **53**, 1021–1033 (1966).
15 Wick, G., Sundick, R. S., and Albini, B., *Clin. Immunopath.*, **3**, 272–300 (1974).
16 Leslie, G. A., and Clem, L. W., *J. exp. Med.*, **130**, 1337–1352 (1969).
17 Leslie, G. A., and Martin, L. N., *J. Immun.*, **110**, 1–9 (1973).
18 Buckley, R. H., in *Immunodeficiency in Man and Animals*, **11** (edit. by Bergsma, D.), 134–142 (Sinauer Associates, Massachusetts, (1975).
19 Albini, B., and Wick, G., *Nature new Biol.*, **249**, 653–654 (1974).
20 Lawton, A. R., Royal, S. A., Self, S., and Cooper, M. D., *J. lab. clin. Med.*, **80**, 26–33 (1972).