

Allergy in the newborn: skin test reactions confirmed by the Prausnitz-Küstner test at birth

HERBERT S. KAUFMAN *Department of Dermatology, University of California School of Medicine, and Department of Pediatrics, Children's Hospital, San Francisco, California*

Summary

Reaginic activity in cord blood with concomitant positive skin tests (confirmed by P-K testing) is reported for the first time (in a 3-hr-old infant). This case illustrates that the atopic state may be present in the neonate.

Introduction

Since the first report of the Prausnitz-Küstner (P-K) reaction in 1921 we have found no reports of such a reaction together with a positive weal and flare skin test in the same newborn. There are reports of positive skin tests in newborns (Balyeat, 1928; Bell & Ericksson, 1931) but none which records simultaneous presence of a positive skin test and reagin cord or venous blood.

During the course of a longitudinal study of ninety-two infants of allergic parents only one infant demonstrated a reproducible positive scratch test and P-K reaction at birth. This report describes the observation.

Case report

K.G. was a full-term male infant weighing 3.5 kg after an uncomplicated vaginal delivery. The placenta appeared normal and the Apgar score was 9. There was no family history of bleeding problems and the mother reported no difficulty during gestation. She had perennial asthma and allergic rhinitis. One month before delivery she was pseudopod skin-test reactive to mixed grass pollens, cat and cow hair. The father was not allergic nor was a 6-year-old sibling. The family kept a pet cat who frequented the entire home.

On physical examination at 3 hr of age, the infant had normal findings; at 5 hr, he was scratch-tested with house dusts Berkeley and Endo, soy, feather, cat and cow hairs, mixed grasses, wheat, egg, cow's milk, and a Coca-saline control before his first feeding. In order to avoid prejudice in testing and interpretation (Kaufman, 1966), antigen was prepared by a technician and labelled only by code number which was revealed after completion of the study. Within 5 min there was a weal reaction to mixed grasses. In 20 min the reaction had increased to + + + + (rating from + to

Correspondence : Dr Herbert S. Kaufman, 2211 Post Street, San Francisco, California 94115, U.S.A.

++++) and additional but lesser reactions were noted to wheat and cow's milk. The skin tests were repeated and reproduced on the infant's back simultaneously with a Coca-saline control and with histamine phosphate (Table 1). A Prausnitz-Küstner test (Stanworth & Kuhns, 1965) was positive to grass pollen antigens (Table 2)

Table 1. K.G. scratch tests at age 5 hr

Antigen*	Weal diameter (mm)	Flare diameter (mm)
Coca-saline	0	0
Grass 1:20	5	15
Histamine PO ₄ (1:37 mg/ml)	3	12
Wheat 1:10	3	10
Milk 1:10	3	10

* Berkeley Biologicals, Berkeley, California.

and to wheat. When the same undiluted serum was heated at 56°C for 4 hr the P-K test was non-reactive. Technical problems prohibited testing by the P-K test to milk or subclass IgG absorption to seek reaginic activity in one of the four classes. The author assumes that reagin is primarily in the immunoglobulin E class of globulins. Immunoglobulins were assayed* in duplicate on cord sera (Table 3).

Table 2. P-K reactions 30 hr after injection of cord serum and 20 min after injection of mixed grass and wheat antigen

Patient's serum dilution	Antigen*	Weal diameter (mm)	Flare diameter (mm)
1:1	Grass	6	18
1:100	Grass	7	16
1:500	Grass	3	11
1:1000	Grass	0	0
Histamine PO ₄ 1:37 mg/ml		5	11
1:1	Wheat	4	13
1:100	Wheat	3	10
1:500	Wheat	0	8
1:1000	Wheat	0	0
Histamine PO ₄ 1:37 mg/ml		4	12

* Berkeley Biologicals, Berkeley, California.

The patient was breast fed from birth and developed atopic dermatitis at 7 weeks of age. Beginning at 17 weeks of age, asthma attacks occurred without pattern or known precipitating cause every 3-4 months, with absence of fever or recognized focus of infection. High concentrations of grass pollen were in the air during the month of birth. Pollination continued for the ensuing 4 months at a lesser concentration. He was retested twice in 10 months, by which time the atopic dermatitis required daily and aggressive care while the asthma attacks were severe and, even with medication,

* IgG, IgA, and IgM: Immunoplates, Hyland Laboratories; IgE: Sandwich solid phase radioimmunoassay.

Table 3. Progressive history

Age examined	Significant history of physical signs	Skin test reactivity	Diet	Immunoglobulin level (mg%)	Treatment
Birth	Normal	+ + + + grass pollens + + wheat + cow milk + + + histamine	None	IgG 1600 IgA 0 IgM 13 (IgE 71 ng/ml*)	None
6 weeks	Fine maculopapular rash on cheeks and lateral aspects of arms	Not done	Breast milk	IgG 1100 IgA 19 IgM 17	None
4 months	Spitting after each feeding	+ cat + + grass pollens + wheat + cow milk	Cow milk	IgG 675 IgA 24 IgM 28	Topical steroids; Benadryl
6 months	First wheezed age 17 weeks; group and wheezing now; atopic dermatitis behind ears	Not done	Cow milk	IgG 690 IgA 41 IgM 82	Topical steroids; Benadryl; Cetaphil, Vioform and Tedral
10 months	Constant runny nose, atopic dermatitis right ear and left antecubital fossa	+ + + cat + + soy, grass pollens, egg, cow milk + Berkeley house dust, feathers, wheat, Endo house dust, cow hair	Multiple formula changes	IgG 810 IgA 50 IgM 165	Topical steroids; Benadryl; Cetaphil, Vioform, Tedral, Elixophyllin

* IgE is reported in nanograms per ml (ng/ml). Normal mean cord blood level = 36 ng/ml (range 16–98 ng/ml) (Johansson, 1968). The newborn serum sample was from cord blood, the remainder from venous blood.

lasted 48–72 hr. In addition, the patient now reacted to all test antigens except the control. No immunotherapy or systemic steroids were given and he received a regular diet (including wheat) for age except for formula changes. A study protocol prevented elimination of milk and other foods from the diet. At age 1 year he continued to have severe allergic symptoms and he was lost to follow-up beyond this time.

Discussion

Work with animal models suggests that the skin test reactivity in this patient may represent passive transfer of grass or wheat reagin from the mother (Ratner, Jackson & Gruehl, 1927a) or active sensitization from wheat or mixed grass antigens (Ratner, Jackson & Gruehl, 1927b) which may have been inhaled through the mother's respiratory tract (Ratner & Gruehl, 1929). The former is unlikely in view of the disparity between skin test reactivity in the mother and the child. The early and numerous test reactions may reflect sensitization *in utero* which became apparent several weeks after birth (Ratner *et al.*, 1927b). The human placenta is the third possible source of immunoglobulin synthesis (Good & Zak, 1956). The allergic activity of serum proteins resides primarily on the subclass of globulins known as immunoglobulin E (IgE). The cord level of IgE in our patient was twice the mean level for newborns but within normal range.

IgE has been reported (Johansson, 1968) in twenty-three random cord bloods analysed, with the mean concentration no different in newborns of allergic compared with non-allergic mothers. In paired maternal and cord sera, the IgE level showed no correlation, suggesting that the source of newborn IgE is not maternal.

The mother's skin test 1 month prepartum, which was negative to wheat (a cultivated grass) but positive to grass pollens, may represent active sensitization of the fetus by an antigen which by-passed and failed to sensitize the mother. There is indirect evidence (Ratner, 1928) of active sensitization from mothers who overindulge in certain foods during pregnancy, whose offspring then experience allergic symptoms on first contact with that particular food.

Positive skin tests (Balyeat, 1928; Bell & Erickson, 1931) and P-K reactions (Allansmith & Buell, 1964) have been reported at birth, but not simultaneously in the same infant. While the fetus is capable of producing IgE, we do not know why there is difficulty in demonstrating the P-K reaction (from cord blood) (Bell & Erickson, 1931; Kuhns, 1965), although the newborn infant is capable of producing a positive P-K reaction from known reaginic donors (Kuhns, 1965; Carey & Gay, 1934). Perhaps the maternal newborn disparity of skin test reactivity is related to a different anaphylactic antibody (Parish, 1970) which may not commonly pass the placenta (Wang *et al.*, 1970). The presence of positive skin tests does not necessarily lead the clinician to infer that a patient is clinically allergic; furthermore, patients with clinical allergy need not have positive skin tests. In our patient, the unexpected positive skin tests and early clinical atopy suggest that the two may be related. This very allergic infant's demonstration of reagin early in life suggests that his immunological vocabulary (Kaufman & Hobbs, 1970) allowed him to say reaginic antibody earlier and louder than usual.

Acknowledgments

The author expresses his thanks to Harry Roth, M.D., for acting as the P-K recipient, and to Sidney Salmon, M.D., for quantitation of serum IgE.

This work was supported in part by U.S. Public Health Service Research Grant No. 2T1A1 63-02 from the National Institutes of Health, Bethesda, Maryland.

References

- ALLANSMITH, M. & BUELL, D.N. (1964) The relationship of gamma-1A globulin and reagin in cord sera. *Journal of Allergy*, **35**, 339.
- BALYEAT, R.M. (1928) Heredity factor in allergic diseases, with special reference to general health and mental activity of allergic patients. *American Journal of the Medical Sciences*, **176**, 332.
- BELL, S.D. & ERICKSSON, Z. (1931) Studies in the transmission of sensitization from mother to child in human beings. Transfer of skin sensitizing antibody. *Journal of Immunology*, **20**, 447.
- CAREY, T.N. & GAY, L.N. (1934) Skin reactions in infants. Susceptibility of the skin of the new born to passive atopic sensitization; comparison with reactions to histamine. *Journal of Allergy*, **5**, 488.
- GOOD, R.A. & ZAK, S.J. (1956) Disturbances in gammaglobulin synthesis as 'experiments of nature'. *Pediatrics*, **18**, 109.
- JOHANSSON, S.G.O. (1968) Serum IgND levels in healthy children and adults. *International Archives of Allergy and Applied Immunology*, **34**, 1.
- KAUFMAN, H.S. (1966) Allergy scratch testing with a uniform technique. Demonstration of a new device. *Annals of Allergy*, **24**, 26.
- KAUFMAN, H.S. & HOBBS, J.R. (1970) Immunologic defects in an atopic population. *Lancet*, **ii**, 1061.
- KUHNS, W.J. (1965) Studies of immediate wheal reactions and of reaginic antibodies from pregnancy and the new born infant. *Proceedings of the Society for Experimental Biology and Medicine*, **118**, 377.
- PARISH, W.E. (1970) Short term anaphylactic IgG antibodies in human sera. *Lancet*, **ii**, 591.
- RATNER, B. (1928) Possible causal factor of food allergy in certain infants. *American Journal of the Diseases of Children*, **36**, 277.
- RATNER, B. & GRUEHL, H.L. (1929) Transmission of respiratory anaphylaxis (asthma) from mother to offspring. *Journal of Experimental Medicine*, **49**, 833.
- RATNER, B., JACKSON, H.C. & GRUEHL, H.L. (1927a) Transmission of protein hypersensitiveness from mother to offspring—passive sensitization *in utero*. *Journal of Immunology*, **14**, 291.
- RATNER, B., JACKSON, H.C. & GRUEHL, H.L. (1927b) Transmission of protein hypersensitiveness from mother to offspring—active sensitization *in utero*. *Journal of Immunology*, **14**, 303.
- STANWORTH, D.R. & KUHN, W.J. (1965) Quantitative studies on the assay of human skin sensitizing antibodies (reagin). I. An examination of factors affecting the accuracy of the Prausnitz-Küstner (P-K) test. *Journal of Immunology*, **8**, 323.
- WANG, A.C., FAULK, W.P., STUCKEY, M.A. & FUDENBERG, H.H. (1970) Chemical differences of adult, fetal and hypogammaglobulinemic IgG immunoglobulins. *Immunochemistry*, **7**, 703.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.