CUTANEOUS BASOPHIL HYPERSENSITIVITY

I. A New Look at the Jones-Mote Reaction, General Characteristics*

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Delayed (cell-mediated) hypersensitivity reactions have been regarded by most workers as a qualitatively homogeneous group (1–3), although well-recognized quantitative differences occur depending primarily on mode of immunization. Classic tuberculin-type delayed hypersensitivity is typically produced by the injection of antigen in complete Freund's adjuvant or in other mixtures containing products of the tubercle bacillus; similar reactivity occurs after dermal contact with simple chemicals and after infections (mycobacterial, fungal, and viral). Delayed-onset skin reactivity can also be produced transiently in a variety of soluble proteins by injection of antigen-antibody complexes or small amounts of the antigen intradermally without mycobacterial adjuvant (4, 5). The latter type of delayed hypersensitivity was termed "Jones-Mote" reactivity by Raffel and Newel (6), who considered it to be qualitatively different from classic delayed hypersensitivity and resembling more closely reactions seen, by those investigators, in humans (7). In the guinea pig, both types of delayed hypersensitivity give a maximum skin reaction at 24 hr, are not necessarily associated with circulating antibody, and can be passively transferred by cells but not by serum (5). Jones-Mote reactivity occurs early in immunization and is evanescent, waning with the appearance of circulating antibody, in contrast to classic delayed hypersensitivity which persists and increases with time. Histologic studies in the past (8–10) have in general shown only quantitative differences between classic delayed and Jones-Mote hypersensitivity reactions, and most investigators have felt the latter to be a weak form of the delayed reaction.

The question of whether the two types of delayed-onset hypersensitivity involve similar or qualitatively different mechanisms was studied using the

azobenzenearsonate hapten system. Hapten-specific delayed hypersensitivity and/or hapten-specific antibody can be produced using different carriers, and so they seemed suitable for exploring the place of Jones-Mote hypersensitivity in the immune economy. We present here evidence in support of Raffel's contention that classic delayed hypersensitivity, produced by antigen incorporated in complete Freund's adjuvant (i.e., with tubercle bacilli), and Jones-Mote reactivity, the delayed-onset skin reactivity produced by antigen in incomplete Freund's adjuvant (i.e., without tubercle bacilli), are qualitatively distinct. Differences between the reactions have emerged with respect to carrier requirements for immunogenicity and for eliciting the skin test, extent of vascular permeability, effect of anti-lymphocyte serum and carrageenan on the skin test, the retest reaction, and the histology of the lesion. A preliminary paper has been published elsewhere (11). The histologic differences between these reactions are fully explored in the following paper (12).

Materials and Methods

Azobenzenearsonate-N-acetyltyrosine (*ABA-Tyr*).—Was prepared as described previously (13).

Azobenzenearsonate-Bovine Serum Albumin (*ABA-BSA*).—Arsanilic acid was conjugated to bovine serum albumin (purchased from Pentex Biochemical, Kankakee, Ill.) by reaction of 10^{-5} moles of the diazotized acid per 10 mg of protein (70 ABA/BSA calculated molecular ratio). Preparation was as described previously (13).

Preparation of Other Conjugates.—Bovine gamma globulin (BGG) obtained from Pentex Biochemical, human insulin (Ins) from Eli Lilly & Co., Indianapolis, Ind., and human gamma globulin (HGG) from Pentex Biochemical were conjugated with arsanilic acid in the same way as that described for BSA.

A polymer of D-glutamic acid, D-alanine, and D-tyrosine (D-GAT) was a gift of Dr. Thomas Gill; a polymer of the L-isomers (L-GAT) was kindly provided by Dr. Paul Maurer; homopolymers of L- and D-tyrosine were purchased from Pilot Labs. Conjugation was carried out in the manner described previously (13).

Immunization.—White, random-bred guinea pigs (400 g) were immunized by injection of a total of 0.1 ml of antigen emulsified in either complete Freund's adjuvant (CFA) or incomplete Freund's adjuvant (IFA) divided equally among the four footpads. IFA was made with 8.5 parts light mineral oil and 1.5 parts Arlacel A; CFA contained 5 mg/ml of killed Mycobacteria in addition.

Skin Testing.—Each group of guinea pigs was skin tested at only one time interval, and reactions were examined at 4, 24, and 48 hr. Tests were intradermal, and the stated dose was injected in a total volume of 0.1 ml of saline. Animals manifesting classic delayed hypersensitivity were most reactive at 3 wk, and this was the usual interval used. Animals immunized with IFA for Jones-Mote reactivity were tested at 4, 7, 10, 14, or 21 days and generally showed good reactions at 7, 10, and 14 days; 4- and 21-day reactions were considerably less intense. Because later skin testing sometimes showed 4 hr erythema, presumably mediated by antibody (12), the 7 day interval was used routinely. In general, hapten-specific sensitivity was elicited by heterologous conjugates of which ABA-L-GAT and ABA-BGG were particularly potent, and ABA-insulin slightly less so. Occasionally, as in the carrageenan and anti-lymphocyte serum studies, the homologous immunizing conjugate was used as skin test antigen to elicit maximal reactions.

Carrageenan Studies.—20 mg of carrageenan (Marine Colloids, Inc., Springfield, N.J.), 10 mg/ml in saline, was injected intraperitoneally 2 hr prior to skin testing in the animals noted.

Anti-Lymphocyte Serum (ALS) Studies.—The stated dose of ALS was injected intraperitoneally in test animals 4 hr prior to skin testing. The ALS was kindly supplied by Dr. John Burke, was produced in rabbits by injection of isolated guinea pig lymph node cells, and was absorbed with guinea pig red cells.

Vascular Permeability Studies.—0.5 ml of 2.5% Evans blue in saline was injected intracardiac in test animals with a 24 hr skin reaction. Blueing of the skin test site was evaluated over the subsequent 60 min.

Retest Reaction.—This phenomenon was described by Arnason and Waksman (14). Animals receiving antigen in CFA were skin tested initially at 3 wk, then they were retested in the same and new sites 6 days later with doses identical with those used in initial skin tests. Similarly, groups of animals receiving antigen in IFA were retested on the same and new sites 4 and 6 days later with identical doses of skin test antigen as used initially. Evolution of reactions was observed at 2, 4, 6, 8, 24, and 48 hr.

RESULTS

Jones-Mote hypersensitivity is defined for the purposes of this study as the delayed-onset skin reaction produced in animals receiving antigen in *incomplete Freund's adjuvant* (IFA). Like classic delayed hypersensitivity, it becomes perceptible at about 6 hr and reaches its height at 18–24 hr. The reaction itself is a well-circumscribed area of erythema, appearing fainter and considerably less indurated than classic delayed hypersensitivity, and is faded or gone at 48 hr. Classic delayed hypersensitivity is produced in this system by immunization with antigen in *complete* Freund's adjuvant (CFA).

Antigenic Requirements for the Production of ABA-Specific Jones-Mote Reactivity.—Extensive experience with ABA conjugates in CFA in this laboratory has revealed that ABA-tyr produces excellent hapten-specific delayed hypersensitivity but no detectable antibody, whereas ABA-BSA produces poor hapten-specific delayed hypersensitivity but good hapten-specific antibody formation. Data in Table I summarize this dichotomy. In animals immunized with ABA-tyr in CFA, delayed reactions increased progressively in intensity for 21 days, at which time they were large and indurated. No antibodies could be demonstrated. Animals immunized with ABA-BSA in CFA, on the other hand, developed a weaker, rather transient delayed reactivity which was maximal at 7 days and waning at 21 days, at which time both PCA and hemolytic antibody were demonstrable in most animals tested.

If it is true that immunization in *incomplete* Freund's adjuvant simply produces milder delayed hypersensitivity, one would expect ABA-tyr to be an excellent immunogen for Jones-Mote hypersensitivity. That such is not the case is shown also in Table I. ABA-tyr in IFA produced little detectable delayed reactivity, whereas ABA-BSA in IFA produced excellent Jones-Mote type reactions. The immunogenic potency of ABA-BSA for ABA-specific delayed hypersensitivity was little affected by the presence of tubercle bacilli, and the

reactions produced by immunization with this material in CFA or IFA were indistinguishable in time course or intensity. The results of these immunogenicity studies suggest that carrier requirements in this system for production of hapten-specific Jones-Mote reactivity more closely resemble those for production of antibody than those for classic delayed hypersensitivity.

TABLE I

Immunogenicity of ABA-tyr and ABA-BSA in Complete and Incomplete Adjuvant

Immunizing conjugate	Delayed skin reactions to:			
	50 μg ABA-BGG			
ABA-tyr (100 μg)	day 4	day 7	day 14	day 21
in IFA	0* (0/6)‡	0 (0/6)	0 (0/5)	0 (0/6)
in CFA	7 ± (3/6)	10 ± (4/6)	16 ++ (6/6)	18 +++ (11/12)
ABA-BSA (100 μg)				
in IFA	3 − (2/8)	12 ± (9/10)	11 ± (7/7)	5 − (5/7)
in CFA	7 − (4/6)	14 + (6/6)	9 ± (5/6)	5 − (4/8)
	50 μg immunizing conjugate at day 7			
ABA-tyr (100 μg)				
in IFA	0(0/5)			
ABA-BSA (100 μg)				
in IFA	16 ± (6/6)			
	Hapten-specific AB formation at day 21			
ABA-tyr (100 μg)	PCA antibody		Hemolytic antibody	
in CFA	0§ (0/20)		0 (0/20)	
ABA-BSA (100 μg)				
in CFA	>1:5 (10/19)		1:80 (18/19)	

* Skin reactions are recorded as average diameter of erythema in millimeters followed by the average degree of induration graded as follows: −, no induration; ±, minimal induration; +, mild induration; ++, moderate induration; +++, marked induration with central blanch.

‡ Number of guinea pigs reacting:number tested.

§ Average titer.

Table II shows the results of skin tests with a variety of ABA conjugates 1 wk after immunizing guinea pigs with 100 μg ABA-BSA in IFA. As in the case of delayed hypersensitivity, the Jones-Mote type reactions seen were hapten-specific in that they could be elicited with approximately equal intensity by ABA conjugates of carriers as diverse as insulin, human gamma globulin, poly-L-GAT, and poly-L-tyrosine. In contradistinction to antibody mediated reactions, however, Jones-Mote reactions could not be elicited by ABA conjugates of D-amino acid polymers, nor could animals be sensitized with such conjugates in IFA.

Since early antibody in the guinea pig has been reported to exhibit carrier specificity (15), an attempt was made to see if L-tyrosine to which ABA was attached in the protein was necessary for full expression of Jones-Mote reactivity. An additional group of guinea pigs was immunized with ABA-BSA in

TABLE II

Carrier Requirements for Eliciting ABA-Specific Jones-Mote Skin Reactions 1 Wk after Immunization in Incomplete Freund's Adjuvant

Immunizing antigen (100 μg)	Skin reactions at 24 hr to 50 μg of:					
	ABA-poly-L-tyr	ABA-poly-D-tyr	ABA- L-GAT	ABA-D-GAT	ABA-ins	ABA-HGG
ABA-BSA ABA-L-GAT ABA-D-GAT	9 ± (5/6)*	0 — (0/6)	12 ± (7/7) 13 ± (7/7) 0 — (0/5)	0 — (0/7) 0 — (0/7) 0 — (0/5)	8 — (5/6)	10 ± (18/22)
ABA-BSA		12 ± (9/12)	ABA-L-GA-D-T 9 — (9/12)	ABA-D-T-gelatin 8 — (9/12)		

* See Table I for grading of skin reactions.

TABLE III

Effect of Carrageenan on Classic Delayed and Jones-Mote Type Skin Reactions

Type of reaction	Mode of immunization	Treatment	Skin reactions at 24 hr to:
			O.T. 1:500
Delayed hypersensitivity	Complete Freund's adjuvant (0.25 mg Tbc)	Control group	11 ++ (8/8)*
		Carrageenan 20 mg i.p.	4 — (7/8)
			ABA-BSA (50 μg)
Jones-Mote hypersensitivity	ABA-BSA 5 μg in IFA	Control group	16 — (7/8)
		Carrageenan 20 mg i.p.	17 — (10/10)

* See Table I for grading of skin reactions.

IFA, and at 1 wk skin was tested with ABA conjugates of a polymer containing D-tyrosine, L-glutamic acid and L-alanine, and an ABA conjugate of D-tyrosine coupled to gelatin (both the generous gift of Dr. Michael Sela). As in the case of classic delayed hypersensitivity, both materials elicited positive reactions, indicating that the reaction was ABA specific and not dependent on the optical activity of the amino acid to which it was coupled.

Effect of Carrageenan on the Skin Reaction.—Carrageenan, a polysaccharide from marine algae, has been shown to interfere with elicitation of classic delayed skin reactions; interference with macrophage activity has been postulated as its mechanism of action (16). Comparison of carrageenan effect in classic delayed and Jones-Mote type reactivity is given in Table III. Tuberculin hypersensitivity is markedly diminished in intensity in carrageenan-treated animals, while identical treatment has no effect on Jones-Mote reactions elicited by ABA-BSA in guinea pigs immunized with ABA-BSA in IFA.

Effect of Anti-Lymphocyte Serum on the Skin Reaction.—Table IV summarizes

TABLE IV

Effect of Anti-Lymphoctye Serum on Classic Delayed and Jones-Mote Type Skin Reactions

Type of reaction	Mode of immunization	Treatment	Skin reactions at 24 hr to:
			O.T. 1:500
Delayed hypersensitivity	Complete Freund's adjuvant (0.25 mg Tbc)	None	12 ++ (12/12)*
		ALS 2 ml	0 − (0/5)
		ALS 1 ml	5 − (3/4)
			ABA-L-GAT (50 μg)
Jones-Mote hypersensitivity	ABA-BSA 100 μg in IFA	None	10 − (11/12)
		ALS 2 ml	0 − (0/5)
		ALS 1 ml	0 − (0/6)

* See Table I for grading of skin reactions.

the effect of ALS on delayed skin reactions. Animals receiving 2 ml of ALS appeared ill, while these receiving 1 ml showed no signs of systemic toxicity. Both Jones-Mote and classic delayed hypersensitivity were almost completely inhibited by both doses of ALS.

Vascular Permeability Studies.—Intravenous injections of Evans blue dye were made 24 hr after skin test with ABA-BSA in guinea pigs 1 wk after immunization with ABA-BSA in IFA. The Jones-Mote skin reactions which were present became pale blue and could be blanched with pressure, indicating a state of hyperemia without dye extravasation; no dye could be seen on the under surface of the skin. On the other hand, most classic delayed skin reactions in animals immunized with CFA showed extravasation of dye within 60 min, confirming the reports of others (17). Injections of dye made within minutes after skin test also failed to show dye extravasation in animals immunized with IFA and tested at 1 wk as above.

The Retest Reaction.—Arnason and Waksman (14) described accelerated

reactivity after reinjection of antigen at sites of previous delayed reactions. We compared retest responses in classic delayed and Jones-Mote hypersensitivity, and the results are given in Table V. Hapten-specific delayed reactions in guinea pigs immunized with ABA-tyr in CFA evolved in the usual time course with nothing grossly visible at 4 hr, erythema without induration at 8 hr, and maximal induration and erythema at 24 hr. When such a site was retested 6 days later a delayed reaction with a much more rapid evolution occurred with maximal induration and erythema already present at 8 hr. A virgin

TABLE V

Comparison of Retest Reactions in Classic Delayed and Jones-Mote Hypersensitivity

Type of reaction	Immunization	Time after skin testing	Skin reactions to 50 μg ABA-HGG		
			Initial	Retest reaction*	Virgin site*
		hr			
Delayed hypersensitivity	ABA-tyr (2 × 10⁻⁶ moles) in CFA 3 wk before testing	2	0 (0/10)‡	0 (0/10)	0 (0/10)
		4	0 (0/10)	10 + (7/9)	er§ (8/9)
		8	12 − (9/10)	14 ++ (9/9)	13 − (9/9)
		24	15 ++ (10/10)	14 + (7/7)	16 + (7/7)
Jones-Mote hypersensitivity	ABA-BSA (100 μg) in IFA 1 wk before testing	2	0 (0/10)	0 (0/10)	0 (0/10)
		4	0 (0/10)	er (6/10)	er (10/10)
		8	8 − (9/10)	9 − (6/10)	13 − (10/10)
		24	9 − (7/9)	10 − (6/8)	14 − (8/8)

* 6 days after initial test.
‡ See Table I for grading of skin reactions.
§ er = slight irregular erythema.

site tested at the same time showed the original time course with maximal reactivity at 24 hr. By contrast, a retest of the site of a Jones-Mote reaction showed little difference in time course or gross appearance from the initial test or another test done at the same time on a virgin site.

DISCUSSION

In the early 1930's Dienes and Mallory (18) compared immediate and delayed type skin reactions and noted that delayed hypersensitivity could be induced to protein antigens in both tuberculous and healthy guinea pigs, although "quantitatively distinctly less intense" in the latter. Delayed reactivity was noted to be characterized by marked infiltration with mononuclear cells. The conclusion was that tuberculin type hypersensitivity is the usual initial stage in the immune response to parenterally introduced protein antigen.

T. Duckett Jones and John R. Mote described in 1934 the development of skin reactivity in humans after repeated intradermal injections of small amounts of rabbit serum proteins (7). A 24 hr "tuberculin type" skin reaction eventually developed in the usual subject, followed after additional testing by an immediate wheal and flare reaction and waning of the delayed component. The immediate, but not the delayed component, was transferable by serum. The delayed reaction was defined as any 24 hr reaction having an erythema of more than 1 cm average diameter, with or without edema.

Observations in rabbits immunized with human plasma and ovalbumin without Freund's adjuvant were reported in 1954 by Gell and Hinde (19), and they included the description of a delayed component to the Arthus reaction characterized by mononuclear cell infiltration. Passive transfer experiments revealed that plasma recipients demonstrated minimal mononuclear infiltration, while cell recipients showed a weak immediate skin reaction and a disproportionately great delayed mononuclear infiltration. These authors suggested that "tuberculin type reactions" could be considered as incomplete immunization procedures.

In 1957, Uhr, Salvin, and Pappenheimer (4) reported the induction of "delayed hypersensitivity" in guinea pigs without adjuvants by the intradermal injection of antigen-antibody complexes containing minute amounts of single protein antigens. Maximal sensitization developed 2–3 wk before detectable circulating antibody. Salvin (5) subsequently demonstrated similar sensitivity following intradermal injection of ovalbumin in Freund's incomplete adjuvant. These authors assumed that the observed delayed hypersensitivity was identical with classic tuberculin type hypersensitivity, and this assumption extended to later studies on desensitization (20) and systemic reactivity (21).

Raffel and Newell (6) in 1958 challenged the assumption that classic delayed reactivity is qualitatively identical with the delayed reactive state produced by antigen-antibody complexes or protein antigen without tubercle bacilli. They pointed out the transient nature of the latter reaction and its apparent relationship to subsequent antibody production, and they suggested that it be distinguished from true delayed hypersensitivity as well as from hypersensitivity reactions of the immediate type. The term "Jones-Mote type reactivity" was proposed for historical reasons. Nelson and Boyden (22, 23) differentiated between delayed reactions to pure protein antigens produced with or without Mycobacteria in adjuvant, and they agreed with Raffel and Newel on definition and terminology of the Jones-Mote reaction. Their studies, however, did not exclude the possibility that Jones-Mote reactivity was simply a milder form of classic delayed hypersensitivity.

Attempts to differentiate classic delayed hypersensitivity and Jones-Mote reactivity by histologic methods have in general revealed only minor quantitative differences (8–10). The Jones-Mote reaction was found to unfold at a slower rate without cellular invasion of epidermis or tissue necrosis, with relatively fewer lymphocytes, and with a greater proportion of mononuclear cells eventually giving rise to plasma cells. In recent reviews of delayed hypersensitivity both Uhr (1) and Turk (2) conclude that differences noted between the Jones-Mote type and the tuberculin type delayed hypersensitivity can be explained by quantitative considerations alone.

Our studies were undertaken initially to establish immunogenic requirements

for Jones-Mote hypersensitivity in the azobenzenearsonate (ABA) hapten system. This system, which gives hapten-specific delayed hypersensitivity following immunization with ABA-tyr (24), seemed particularly well suited for exploration of the relationship of Jones-Mote reactivity to antibody-mediated and cell-mediated hypersensitivity without detectable antibody formation. ABA-BSA in CFA, on the other hand, produces poor hapten-specific delayed hypersensitivity but good ABA-specific antibody (25). If Jones-Mote reactivity were simply mild delayed hypersensitivity, then ABA-tyr in IFA should produce good Jones-Mote lesions, whereas ABA-BSA in IFA should produce little if any Jones-Mote reactivity. Our results proved otherwise, leading to the conclusion that immunogenicity requirements for Jones-Mote hypersensitivity resemble those for antibody formation rather than for true delayed hypersensitivity.

Another possible explanation of the above findings might be that antibody production "turns off" or conceals delayed skin reactivity, and that ABA-BSA is simply a better immunogen for both delayed hypersensitivity and antibody production. Repeated attempts to inhibit expression of delayed hypersensitivity by antibody have been unsuccessful, and in fact excellent delayed hypersensitivity in the presence of antibody occurs after concurrent immunization with ABA-tyr and ABA-BSA.[1] This alternate explanation, then, appears to be untenable.

Turk and Heather (26) have concluded from a histological study of lymph nodes that Jones-Mote hypersensitivity is accompanied by lymph node changes typical of those in animals developing contact sensitivity, the homograft reaction, or B.C.G. vaccination. These changes involve a high concentration of large pyroninophilic cells ("immunoblasts") in paracortical areas 4 days after sensitization. Hall (27) has found large numbers of similar cells in circulating lymph several days prior to the appearance of medullary plasma cells and antibody formation, after immunization with many types of antigen. These mobile pyroninophilic immunoblasts disseminate widely throughout the body. What their role is in delayed hypersensitivity remains to be established, but it is tempting to speculate that they are the antigen-recognizing cells in the Jones-Mote reaction.

The passive transfer of Jones-Mote reactivity has been achieved with sensitized lymphoid cells but not serum (5), and we have confirmed these results. Our results with synthetic carrier polymers indicate that *preformed* antibody plays no role. The D-polymer carrier of ABA, while capable of eliciting skin reactions mediated by preformed antibody (e.g., PCA and Arthus reactions [13]), is unable to elicit the Jones-Mote skin reaction in sensitized animals. That this is probably not due to carrier specificity of some type of early antibody is

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[1] Leskowitz, S. and H. J. Schwartz. Unpublished observation.

seen by the positive reactions to ABA conjugates of D-tyrosine in L-amino acid carriers (Table I). As long as the carrier is immunogenic per se reactions are specific for the ABA group.

The experiments using anti-lymphocyte serum, while not conclusive, point to requirements for some type of lymphocyte population in Jones-Mote reactivity as in classic delayed hypersensitivity. The results with carrageenan, however, suggest that a macrophage population sensitive to its action does not make a significant contribution to Jones-Mote as contrasted with delayed hypersensitivity reactions. The Evans blue dye studies indicate the Jones-Mote reaction to be a simple vascular hyperemia rather than the result of increased vascular permeability. The significance of the absence of a retest response in Jones-Mote skin sites cannot be evaluated since so little is known of the mechanism of this phenomenon in delayed reaction sites. Nevertheless, it is another point of distinction between the two types of reaction.

These results taken together suggest a mechanism for Jones-Mote reactions involving an active stimulatory cellular response requiring an immunogen acting perhaps on the circulating immunoblasts released from lymph nodes (28). This stimulation may result in differentiation into antibody producing cells or, more probably, the release of mediators producing the unique cellular response involving the accumulation of basophils seen in this type of reaction (12).

The current assumption that cell-mediated delayed hypersensitivity is a qualitatively homogeneous response is surprising in view of the well-established heterogeneity of the antibody response. Understanding of classic cell-mediated tuberculin hypersensitivity has been facilitated by in vitro systems, showing that lymphocytes are antigen-responsive cells capable of elaborating substances which attract and activate macrophages (29). In the following paper (12) we demonstrate a significantly different histologic pattern of cellular response for Jones-Mote reactions presumably involving a different mechanism. The major finding is the prominence of basophils in reactions elicited early after immunization with IFA. Since the reactions originally described by Jones and Mote (7) were operationally different and of unknown histology, we propose that the reactions studied here and in the subsequent paper (12) be designated "cutaneous basophil hypersensitivity." Several immune responses are now considered to be examples of classic delayed hypersensitivity; these include homograft rejection, tumor immunity, autoimmune disease, and contact dermatitis. Further clarification of the role played by basophil cellular responses in these and other immunologic phenomena is vital.

SUMMARY

Jones-Mote reactivity, defined as a delayed-type skin reaction, occurs transiently early in the course of immunization with protein antigens or hapten

conjugates with or without the adjuvant effect of tubercle bacilli. The skin reaction is typically a flat, well-circumscribed erythema with little induration beginning at about 6 hr, reaching a peak at 18–24 hr, and fading or gone at 48 hr.

Immunogenic carrier requirements for hapten-specific Jones-Mote hypersitivity resemble those of antibody production rather than of classic delayed hypersensitivity. Skin test antigen requirements indicate that the Jones-Mote reaction involves an active stimulatory response rather than combination with preformed antibody, since ABA conjugates of nonimmunogenic D-polymers do not work. Studies with ALS and carrageenan suggest that the lymphocyte is an important contributor to the reaction, but the macrophage is not.

Because the reactions studied here are operationally different from those described by Jones and Mote and because they have a characteristic histology, the term "cutaneous basophil hypersensitivity" is proposed.

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