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COMPARISON OF INTRADERMAL TESTS WITH AGGLUTINABILITY AND CERTAIN IN VITRO TESTS OF STREPTOCOCCI, STAPHYLOCOCCI, MICROCOCCUS CATARRHALIS, AND COLON BACILLI ISOLATED FROM PERSONS SUSPECTED OF HAVING CHRONIC INFECTION*

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INTRADERMAL tests have been used widely, not only for the differentiation of "focal infection" bacteria, but also in the selection of bacteria for the preparation of autogenous vaccines. The literature is too voluminous to be reviewed here. The following papers, however, have a special bearing on the subject.

Feinberg[1] presented an excellent critique of the limitation of skin tests in allergy.

Steinberg and Wiltsie[2] obtained reactions with *B. coli* toxic filtrate in all 60 normal children and all 40 normal adults. These results are similar to those obtained by workers in other allergens. For example, Grow and Herman[3] obtained 55.5 per cent positive results with common allergens in a group of 150 normal individuals.

Inconclusive results have been reported also in persons with different diseases. Steinberg and Wiltsie[2] found that the skin reaction to *B. coli* was not related to the presence of infection. Four of 11 patients with pyelitis did not react to *B. coli* toxic filtrate, and 5 of 11 did not react to *B. coli* vaccine. They concluded that "under the conditions of these experiments, the skin reaction for the determination of the presence of colon bacillus infection is of uncertain value." Solis-Cohen[4] concluded that "There probably is no relationship between hypersensitiveness in the host to the exogenous and endogenous toxins of a given organism and the pathogenicity of such organism for that host." His conclusion that intracutaneous tests are unreliable for selecting bacteria for vaccines seems to have been shared by most recent writers on the subject, although many of them, like Moore,[5] admitted the fallacy of the tests but concluded that they are "a very important factor as an aid to diagnosis of allergic diseases."

Much of the published data is difficult to interpret because of errors in bacteriologic diagnosis or the use of indefinite bacteriologic names. For

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example, one writer stated that 105 of his 133 strains of hemolytic streptococci were isolated from the gastrointestinal tract. It is more likely that many of these cultures were hemolytic enterococci, which are mostly nonpathogenic and possess properties distinct from other hemolytic streptococci. Other workers refer to any intestinal streptococcus as *Streptococcus fecalis* or to small, hemolytic surface colonies as hemolytic streptococci. Many of the latter may be alpha hemolytic or alpha prime streptococci, or may not even be streptococci.

Many of the published reports concerned work which was inadequately controlled. One writer reported using an average of only 3.6 tests per patient and 2.9 tests per control case.

Finally, the difference between the proportion of positive reactions in patients and in the controls does not show a marked contrast. In comparing patients with irritable colon with normal individuals, Mateer and Baltz[6] obtained diameters of 4.4 and 3.0 cm., respectively, with *B. coli communis;* 4.5 and 2.7 cm. with *B. coli communior;* 2.7 and 1.0 cm. with nonhemolytic streptococci; and 2.4 and 1.0 cm. with *Staphylococcus aureus.* The tests with *B. coli communis* were positive in 95 and 65 per cent, with *B. coli communior* in 96 and 69 per cent, with nonhemolytic streptococci in 62 and 21 per cent, and with *Staphylococcus aureus* in 49 and 50 per cent of patients and controls, respectively. Mateer and co-workers[8] obtained similar results.

Short, Dienes, and Bauer[7] maintained that variations in the skin reactions may be explained by differing irritability of the patients' skins, natural toxicity of the bacterial species, or possibly by a sensitization to certain bacterial groups.

Mateer and Baltz[6] claimed that the reaction decreased after immunization with the specific vaccine. However, their report indicates that the average reactions to *B. coli* were reduced only from 4.7 to 3.1 cm. in 12 patients immunized with *B. coli.* Steinberg and Wiltsie[2] found an average area of 9.7 by 6.5 cm. before, and 3.9 by 2.3 cm. after immunization with *B. coli.*

Since certain in vitro tests have been shown to give results parallel with certain pathogenic properties of the cultures,[9-15] it was thought that these in vitro tests might be useful in comparing the results of intradermal tests. Agglutination tests were used for comparison also. A series of 305 smooth cultures was tested.

For the intradermal tests the bacteria were suspended in 1.0 per cent phenol in normal saline to make concentrations of 1 billion per c.c., and 0.05 c.c. was injected intradermally on the forearm. The results were read the following day.

The technique of the agglutination tests is described elsewhere.[16]

Pigment, hemolysis, and coagulase tests[9] were used as in vitro tests of staphylococci; resistance to the bactericidal action of fresh, diluted, defibrinated guinea pig blood[10, 11, 15] was used for streptococci; the electrophoretic migration velocity[12, 13] was used for the colon group; and the crystal violet agar reaction[14] was used for *M. catarrhalis.*

The results of the comparative tests are listed in Table I. There was agreement between intradermal and in vitro tests in 83 per cent of *M. catarrhalis*

cultures, 84 to 87 per cent of staphylococci, and in 70 per cent of gamma type streptococci. Other groups showed agreement in less than 57 per cent of the tests.

TABLE I

RELATION BETWEEN INTRADERMAL TESTS, AGGLUTINABILITY AND IN VITRO TESTS OF PROBABLE PATHOGENICITY OF CULTURES ISOLATED FROM PERSONS SUSPECTED OF HAVING CHRONIC INFECTION

ORGANISM	CULTURES GIVING POSITIVE INTRADERMAL TESTS			CULTURES GIVING NEGATIVE INTRADERMAL TESTS			PER CENT AGREEMENT BETWEEN SKIN TESTS AND IN VITRO TESTS	PER CENT AGREEMENT BETWEEN SKIN TESTS AND AGGLUTINABILITY
	NUMBER TESTED	IN VITRO POSITIVE	AGGLUTINABLE	NUMBER TESTED	IN VITRO NEGATIVE	INAGGLUTINABLE		
B. coli	19	2	5	11	10	10	40	50
A. aerogenes	9	5	2	2	0	2	45	36
Paracoli	4	0	0	4	4	2	50	25
Enterococci	4		2	19		19		91
Strep., gamma	3	0	1	14	12	14	70	88
Strep., alpha	11	5	1	105	58	65	54	57
Strep., beta	4	4	0	3	0	2	57	28
M. catarrhalis	1	0	1	5	5	5	83	100
Staph. albus	7	4	1	57	50	43	84	69
Staph. aureus	8	8	5	15	11	11	87	70

There was agreement between intradermal tests and agglutinability in 91 per cent of enterococci, 88 per cent of gamma type streptococci, 100 per cent of *Micrococcus catarrhalis,* and 69 to 70 per cent of staphylococci. Other groups showed agreement in less than 57 per cent of tests.

CONCLUSIONS

Intradermal tests of bacteria isolated from patients suspected of having chronic infection were compared with (1) agglutination reactions of the strains using the serum of the person from whom the cultures were obtained and (2) in vitro tests which had been shown previously to have been parallel with certain pathogenic properties of the cultures.

The intradermal tests showed agreement with either agglutinability or the in vitro tests in more than 70 per cent of *Micrococcus catarrhalis,* staphylococci, gamma type streptococci, and enterococci.

There was less than 57 per cent agreement with either test in alpha and beta type streptococci, *B. coli, Aerobacter aerogenes,* and paracoli.

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