

## “PROCUTINS” AND “ANTICUTINS”\*

MAX PINNER, MOE WEISS, AND A. C. COHEN

During the early phase of bacteriological-immunological work on tuberculosis, many answers to unsolved questions were sought in serological reactions and in antigen-antibody relations, demonstrable either *in vitro* or *in vivo*. A product of that time is the work of Pickert and of Löwenstein<sup>3</sup> on the so-called “procutins” and “anticutins.” They were considered in terms of antibodies specific to tuberculin. These authors observed that in appropriate mixtures of Old Tuberculin and serum, the skin reactivity of tuberculin was either enhanced (procutins) or decreased (anticutins). These “cutins” were related to the immunological status of the serum donors. The theories built on such studies have long since gone the way of all immunological theories in tuberculosis, the main basis for which were humoral “antibodies.” There would be no useful reason to revive work along these lines, were it not for the fact that, relatively recently, Martenstein<sup>4</sup> found that the high frequency of anergy to tuberculin in sarcoidosis is apparently related to anticutins. He believed that patients with sarcoidosis did not react to tuberculin because they carried anticutin in their sera. In other words, humoral, tuberculin-neutralizing factors prevented the common manifestation of an actually existing allergy. This theory received further support by the observation of Jadassohn<sup>2</sup> that (1) rats respond to the introduction of tubercle bacilli by the formation of lesions that greatly resemble histologically the sarcoid lesions in man, and (2) rat serum contains tuberculin-neutralizing factors (anticutins).

In a previous publication, it was mentioned that anticutins had been demonstrated in three patients with sarcoidosis. It was well realized that the findings in three patients could not carry much weight, but more patients with sarcoidosis were not available at the time. Furthermore, it remained to be determined whether sera from normal persons and from tuberculous patients exerted any demonstrable effect upon the skin-reacting element in O T.

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\* From the Montefiore Hospital Country Sanatorium, Bedford Hills, New York.

### *Technic*

In all our tests, a constant technic was used: equal amounts of O T 1:5,000 and undiluted serum were mixed under sterile precautions, incubated for a minimum of 2 hrs., and 0.1 cc. of the mixture was injected intracutaneously in a known tuberculin-reactor. Simultaneously a mixture of O T 1:5,000 and serum diluted 1:10 with saline was injected. For comparison, O T 1:10,000 was similarly injected. It will be noted that in each of the three injections, 0.1 cc. of O T 1:10,000 was present, that the first mixture contained in addition 50 per cent serum, the second 5 per cent serum, and the third no serum. The skin reactions were measured 48 hrs. following the injections. Control injections were made with 50 and 5 per cent serum in saline.

### *Results*

It was first necessary to determine what differences in the size of skin reactions could be accepted as significant and not caused by errors inherent in the technic. We performed, therefore, duplicate Mantoux tests on 190 tuberculin-reactors, giving the two injections in symmetrical locations on the flexor surface of both lower arms. Minor differences in the size of the resulting skin reactions are frequent and must probably be explained by unavoidable differences in the volume injected and by equally unavoidable differences in the depth of the injections, although all tests were ruled out in which the injection did not produce a pale elevated bleb.

Simultaneous, duplicate tests with identical dosage at symmetrical sites were done on 190 persons, most of them tuberculous patients. All but three duplicate tests showed less than a 50 per cent difference in the diameters. On this basis, it was assumed that differences greater than 50 per cent between the O T reaction and one or both O T + serum reactions, indicated the presence of "anticutins" or "procutins." Sera producing less than a 50 per cent change in diameter of the skin reaction were termed inert. The 50 and 5 per cent serum injections produced only occasionally slight reactions which had usually more or less completely disappeared in 48 hours.

An attempt was made to correlate the presence of cutins with the dynamic status of the tuberculosis of the donors' sera. Table 1 shows the results.

It will be seen (1) that, regardless of the type of tuberculosis present or of the lack of tuberculosis, a considerable percentage of sera contains "procutins," (2) that no definite trend is discernible

TABLE 1

THE INCIDENCE OF "PROCUTINS" AND "ANTICUTINS" IN THE SERA OF TUBERCULOUS PATIENTS, ACCORDING TO THE STATUS OF THE DISEASE, AND IN NORMAL PERSONS

<i>Type of disease</i>	<i>No. of cases</i>	<i>Procutins</i>		<i>Inert</i>		<i>Anticutins</i>	
		<i>No.</i>	<i>%</i>	<i>No.</i>	<i>%</i>	<i>No.</i>	<i>%</i>
Progressive .....	38	15	40	23	60	0	0
Quiescent .....	39	17	44	20	51	2	5
Retrogressive .....	36	22	61	11	31	3	8
Arrested .....	21	9	43	9	43	3	14
Apparently cured .....	35	12	34	19	54	4	12
Tuberculin pos. normals..	62	25	40	35	57	2	3
Tuberculin neg. normals..	22	6	27.3	14	63.6	2	9.1
Total .....	253	106	41.9	131	51.8	16	6.3

suggesting an intelligible relation between procutins and the dynamic status of the disease, (3) that anticutins occur quite rarely in all groups of patients, save those with progressive disease, (4) that anticutins are of practically the same frequency in the arrested cases, in those apparently cured, and in tuberculin-negative persons (mostly babies).

The occurrence of procutins or anticutins does not suggest any relation to those criteria of the disease that might be manifestations of the patients' immunological condition.

Next, the serum donors were grouped, according to their skin-tuberculin tests, into two classes, those with high and those with low allergy. In an entirely arbitrary way, we designated as highly allergic all persons who had a reaction 2 cm. or more in diameter to an O T dilution of 1:10,000 or less, and as slightly allergic those persons who had a reaction of 1 cm. or less in diameter to an O T dilution of 1:1,000 or more. The results are presented in Table 2.

A definite trend is no more evident in Table 2 than it was in Table 1, and the conclusion appears justified that "procutins" and "anticutins" are not with any discernible regularity associated with different degrees of allergy in the serum donors.

In addition, we had, through the courtesy of a number of colleagues, the opportunity of testing the sera of eight patients with

TABLE 2

THE INCIDENCE OF "PROCUTINS" AND "ANTICUTINS" ACCORDING TO THE ALLERGIC STATUS OF THE SERUM DONORS

Degree of allergy	Number tested	Procutins		Inert		Anticutins	
		No.	%	No.	%	No.	%
High allergy .....	65	27	42	34	52	4	6
Low allergy .....	23	9	39	10	44	4	18
No allergy .....	22	6	27	14	64	2	9

sarcoidosis, not included in Tables 1 and 2. In only one of these were anticutins demonstrated; four showed procutins. Adding to these eight sarcoid sera the three previously reported, all of which contained "anticutins," we have demonstrated anticutins in four out of eleven sarcoid sera, that is, in about 36 per cent. A sample of some 250 sera cannot be compared with one of 11. The real significance of "anticutins" in sarcoidosis must, therefore, remain an open question. However, it is probably important to point out that in our experience, at least, only about one-third of sarcoid patients contained "anticutins," a much lower percentage than that of negative tuberculin-reactors in this disease.

Finally, the sera of 11 rats were tested. Here, the technic was modified so that the serum-O T mixture was injected at least 24 hrs. after mixing so that sterility tests were available before injection. All 11 rat sera were found to be inert.

### Conclusions

1 So-called "anticutins" are demonstrable in the sera of a small percentage (5 per cent) of normal persons and of tuberculous patients. They do not appear to be significantly related to the dynamic status of the donor's tuberculosis.

2 "Anticutins" occurred in about 36 per cent of patients with sarcoidosis. Whether or not this is a frequency that is immunologically and diagnostically significant cannot be decided on the basis of the available material. However, "anticutins" are considerably rarer than is anergy in sarcoid patients.

3 So-called "procutins" were demonstrated in nearly half of the persons examined. They, like the "anticutins," do not appear

to be significantly related to the dynamic status of the donor's tuberculosis.

4 Eleven rat sera examined contained neither "procutins" nor "anticutins."

## REFERENCES

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