

The question of whether this apparent increase in nuclear binding in vitro resulted from an increase in the affinity, stability, or synthesis of the nuclear "receptor" or from the transfer of a T_3 -cytosol receptor complex remains to be defined.

The nuclear binding of [125 I] T_3 after incubation of hormone with intact GH₁ cells (3) is similar to that observed by Oppenheimer and colleagues (4, 5) after injection of [125 I] T_3 into rats. As we have demonstrated, putative receptors for T_3 detected in vitro are similar in isolated nuclei and soluble nuclear extracts of rat liver, kidney, and GH₁ cells. This suggests that our studies of thyroid hormone action in cell culture might serve as a valid model for studying the mechanisms of thyroid hormone-receptor interaction as well as thyroid hormone regulatory effects in vivo.

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Leprosy: Confirmation in the Armadillo

Abstract. *Bacteria isolated from lesions of lepromatoid leprosy in the armadillo were studied in comparison with Mycobacterium leprae isolated directly from human lepromatous leprosy lesions. Three methods were used to show that the bacteria from the lesions of the armadillo were identical to those of the human lesions: (i) extraction of the bacteria with pyridine and subsequent staining with various techniques, (ii) the competence in clearing bacilli (CCB) test, and (iii) the Mitsuda test.*

Leprosy is an important public health problem in many parts of the world. It is generally considered to be one of the oldest diseases known to afflict mankind and yet, ironically, it is one of the least understood. Only limited knowledge is available concerning the epidemiology of the disease (such as modes of transmission and susceptibility) as well as the most effective means to control and treat it. This is the result of not being able to grow the causative agent, *Mycobacterium leprae*, in culture and also, until recently, of not having a suitable animal system in which to study the disease. Although multiplication of the organism will occur in the mouse footpad, the lesions that result are microscopic and no gross evidence of disease can be seen in immunologically intact rodents.

Leprosy is a very unusual disease

with respect to the different courses it takes in humans and the large variety of lesions that it presents. The organism *M. leprae* is an intracellular parasite and as such its growth is controlled by the cell-mediated side of the immune response. While many individuals are immunologically capable of localizing the disease and manifest the more benign type known as tuberculoid leprosy, some individuals are unable to eliminate the organism and thus develop the severe disseminated form known as lepromatous leprosy. In addition, there is a large group that falls somewhere between these two polar forms immunologically, and such patients develop a dimorphous form known as borderline leprosy. Because of these variations in host response, leprosy is considered by many to be the most complete model of the gran-

ulomatous diseases, and the study of it could therefore result in significant contributions to an understanding of cell-mediated immunity and its role in other infectious processes.

Storrs (1) and Kirchheimer and Storrs (2) were able to produce lesions in the nine-banded armadillo (*Dasypus novemcinctus*, Linn.) after inoculation of *M. leprae* isolated from a patient with lepromatous leprosy. Lesions containing large numbers of acid-fast bacilli were seen and histopathologic examination showed changes that were consistent with a diagnosis of lepromatous leprosy (3).

In order to ascertain that the organisms isolated from infected armadillos were indeed *M. leprae* and not some other closely related mycobacteria, we decided to compare them with *M. leprae* isolated from human cases. This comparison was done with the use of tests that had been shown to be valid for differentiating *M. leprae* from other mycobacteria.

The infected armadillo tissue which we studied had been taken from two infected animals (4): armadillo 5, which had been inoculated 31 months prior to its death with *M. leprae* from a human lepromatous case, and armadillo 18, which had been inoculated 26 months before its death with organisms obtained from a strain of human *M. leprae* that had been passaged through the footpads of mice.

For the identification of the mycobacteria isolated from armadillos 5 and 18 we used three methods; these methods confirmed that the bacilli found in infected armadillos are *M. leprae*.

1) Effect of pyridine treatment on acid-fastness, Baker's stain for phospholipids, and fluorochrome staining with the use of auramine-rhodamine: Of all other known mycobacteria, only *M. leprae* completely loses its ability to be stained by the above three methods after 2-hour treatment with pyridine (5). To determine the reaction of the mycobacteria from the armadillo, smears and sections were prepared from each of the armadillo specimens, from human lepromatous lesions, from murine leprosy lesions (*M. lepraemurium*), and BCG (bacillus Calmette-Guérin). The specimens were treated with pyridine for 2 hours and stained along with untreated control slides. All slides were read "blind," and it was found that the organisms from the armadillos behaved identically to human *M. leprae*; that is, they lost their acid-fastness, their ability to be stained with

Baker's stain, and their capacity to retain auramine-rhodamine stain. As was reported earlier (6), *M. lepraemurium* and BCG retained their staining capabilities after treatment with pyridine.

2) Competence in clearing bacilli (CCB) test: This is a test that was developed in our laboratories and in which an antigen similar to the Mitsuda antigen is used (6). It differs from the Mitsuda antigen in that it contains a much larger number of heat-killed *M. leprae*, so that it produces a macroscopic nodule in lepromatous patients 30 days after intradermal inoculation. Biopsy of the nodule shows typical lepra cell granulomas composed of macrophages containing large numbers of acid-fast bacilli. For this test, antigens were prepared from each of the armadillo tissues along with *M. leprae* obtained from human lepromatous tissue. Each preparation contained 6.4×10^8 organisms and was injected intradermally into 20 lepromatous patients. Some of these patients were bacteriologically negative after several years of sulfone therapy while others were sultone-treated patients with active lesions.

The two antigens prepared from armadillo tissues gave the same responses in these individuals as the antigen prepared from human lepromatous tissue; that is, a nodule had formed at the injection site of each patient 30 days after inoculation. Biopsy of all three nodules in each patient showed large numbers of macrophages containing numerous acid-fast bacilli.

3) Mitsuda test: Antigens were prepared with material from armadillo 5 and from human material taken from lepromatous patients. The inoculums were adjusted to a concentration of 4.0×10^7 organisms per milliliter. This material was injected into the same 20 patients used for the CCB test, as well as into 7 patients with diagnosed tuberculoid leprosy. Each patient was inoculated with 0.1 ml intradermally on the surfaces of the forearm. At 30 days, the lepromatous patients showed no reaction to either the antigen from the human lepromatous patients or the antigen prepared from the injected armadillo tissue. The tuberculoid patients, however, gave positive reactions to both preparations. Thus, the Mitsuda response with armadillo antigen as compared to human antigen was the same in both lepromatous and tuberculoid patients. This is an important finding

since leprologists are in general agreement that one of the primary proofs for the identification of *M. leprae* is that the organism in question produces the same response as *M. leprae* from human leprosy when inoculated into lepromatous and tuberculoid patients.

The results of these tests provide definite proof that the acid-fast organisms isolated from armadillos after experimental inoculation with *M. leprae* are identical to *M. leprae* isolated directly from human lepromatous patients.

In addition, we have recently transmitted leprosy to another species of armadillo. The details of this will be reported elsewhere (7).

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Perception of Letters in Words: Seek Not and Ye Shall Find

Abstract. *Subjects perceive a letter in a briefly presented word more accurately when they attend to the whole word than when they focus their attention on just the letter they want to see.*

Until recently, most accounts of visual information processing have dealt primarily with isolated stimuli (such as single letters) or arrays of unrelated stimuli (such as random letter strings) (1). Outside of the perception laboratory, however, stimuli are usually related to one another; in particular, they often fit together to form larger, coherent wholes.

It has been demonstrated that belonging to a larger whole can have an important effect on perceptual processing. The letters in a word are perceived more accurately than a single letter alone, even when perception is tested by a forced-choice procedure that eliminates any guessing advantage for words (2, 3). For instance, subjects are more accurate in deciding whether a brief exposure of the word COIN was COIN or JOIN than whether a brief exposure of C was C or J.

This finding rules out the possibility that what we see when we perceive a word is a set of independently identified letters. Letters in a word are simply perceived too accurately for this to be the case (4). The processing of any

given stimulus letter must depend critically on the larger stimulus of which it is a part.

Previous demonstrations of this word-letter phenomenon leave open an important question. Is it due simply to the nature of the stimulus? Or must the subject actively attend to the whole stimulus word for perception of a letter to be enhanced? If attention to the whole is necessary, we reasoned that the word-letter phenomenon could be obtained using the same stimulus under two different instructions: to look at just one letter position in the word, or to look at the whole word. Looking at just the first letter in COIN as an individual letter should reduce perceptibility of the C compared to looking at the whole word COIN. This seemingly paradoxical result is exactly what we found.

Sixteen subjects (University of Pennsylvania students) viewed very brief exposures of four-letter words. Each word was typed in capital letters with a half space between letters (5) and subtended 1.90° by 0.42° of visual angle. Stimuli were presented in a two-field tachistoscope with a random con-