ADRENAL CORTEX

Transactions of the Fifth Conference
November 4, 5 and 6, 1953, Princeton, N. J.

Edited by
ELAINE P. RALLI, M.D.
ASSOCIATE PROFESSOR OF MEDICINE
NEW YORK UNIVERSITY
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NEW YORK, N. Y.

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JOSIAH MACY, JR. FOUNDATION
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JANET FREED LYNCH, *Assistant for the Conference Program*†

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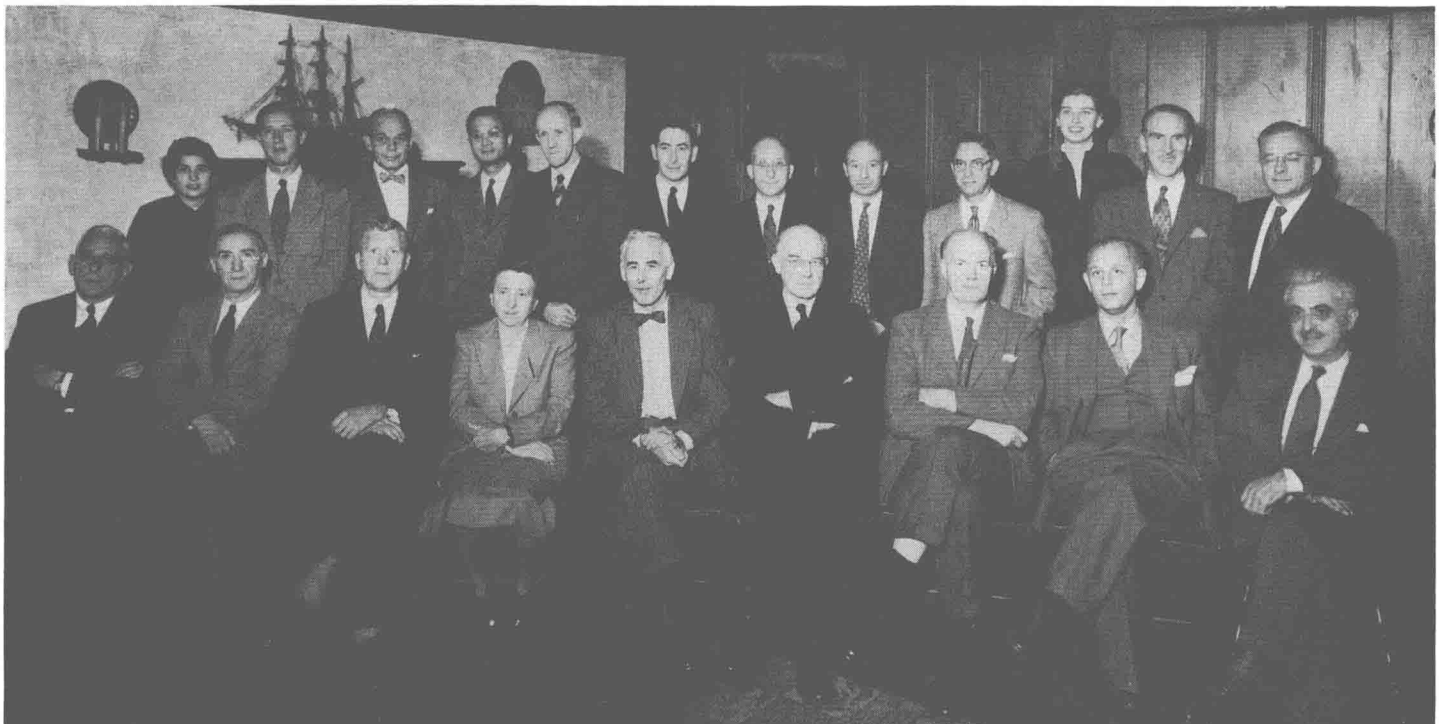

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Fifth Conference on Adrenal Cortex

THE JOSIAH MACY, JR. FOUNDATION CONFERENCE PROGRAM

WHEN I WAS on a destroyer out at Bikini in 1946 I was fascinated listening to our radio operator as he tested communication equipment. He would ask another ship through his radio, "How do you hear me?" and the answer often would come back, "I hear you Nine-Nine-Nine." That meant that everything was satisfactory. Of the three nines, one was for intensity, one for clarity, and one for meaning.

The Josiah Macy, Jr. Foundation has organized and devoted a large portion of its resources to the support of its Conference Program because the officers are cognizant of the fact that there is considerable obstruction to communication and mutual understanding across the disciplines and specialties, and that this, in fact, is one of the major factors delaying scientific advance. We feel that there are psychological, as well as semantic factors contributing to the difficulty of communication; people, even in arguments with one another, are too much inclined to make statements *at*, rather than to communicate *with*, others. I think that we are inclined to forget, though, that the real question is, are these words and statements those which are likely to convey to the listener the whole or even a small part of what I would like to express.

I have a feeling that we should be very much concerned with the other fellow's receiving set and not only with our own transmitter. If the other person doesn't seem to understand us, it may not be enough merely to increase the power of our transmission; we must try to find the obstruction in his receiving set, and see what kind of filters and resistors he uses. So, if we call out to the interprofessional No-Man's-Land, "How do you hear me?" and the reply comes back, "I hear you Nine-Nine-Nine," we have the beginning of communication. What we try to do in these conferences conducted by the Foundation is to set the stage for meaningful communication.

With the accelerating rate at which new knowledge is accumulating and with the increasing recognition that nature is of one piece, it becomes evident that the continued isolation of the several branches of science from one another is a serious obstacle to scientific progress. Nowhere in science is the need for "combined opera-

tions" more evident than in medicine. Today, to be effective, medical research and practice must embrace data from all the disciplines including nuclear physics at one end of the spectrum and cultural anthropology at the other, for advances in one field are frequently dependent upon knowledge derived from quite another discipline.

Although the fertility of the multidiscipline approach is thus recognized, universities, and scientific societies and journals which are usually restricted to one small area of a field in their coverage, have not yet made adequate provision for channels of interdisciplinary communication. We do not wish to compete with the formal scientific meetings or with the scientific journals which have established patterns and formats for the presentation of material. Our purpose at the meetings is to keep an informal atmosphere and to encourage the exchange of methods, research plans, concepts and difficulties, which cannot be done if there is formal speech making.

The Foundation has endeavored to meet the need for interdisciplinary communication by bringing together for a series of two-and-a-half day annual conferences a small group of investigators, representing in so far as possible all the branches of science related to a chosen problem. Participants in these informal conferences over a five-year period develop a feeling of friendship, trust and mutual respect which in turn promotes communication, cross-fertilization of ideas and cooperation. The success of such an endeavor, however, is dependent upon full participation of all members in the discussion. Accordingly attendance at any conference is limited to twenty-five.

Under the guidance of Dr. Willard C. Rappleye, President of the Foundation since 1942, the Conference Program has been gradually expanded and enlarged until during 1953 it included twelve different groups which meet annually to discuss a wide variety of problems in the field of medicine and the closely related disciplines. Our plan is to discontinue the meetings of each group at the end of five years.

In order to share with a wider group of investigators and students the essential quality of these conferences and to give others an insight into the functions of the scientific mind, the informal nature and tempo of the discussions, as far as possible, are preserved in the published transactions.

FRANK FREMONT-SMITH, M.D.,
Medical Director

THE SALT AND WATER FACTOR OF THE ADRENAL CORTEX*

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Mayo Clinic

YOU ARE ALL I think, familiar with the works of Tait, Simpson, and Grundy (1), and Woodford (2) in England. More recently Reichstein and his associates (3), have announced the isolation of what has tentatively been called "electrocortin." Dr. Reichstein has indicated to us that electrocortin is not a satisfactory name, but feels that a better name should at least await the determination of the structure.

We were a little behind Reichstein in announcing the crystallization of our compound, which appears to be the same one that he and his associates have isolated. A lack of materials on both sides has prevented a comparison of the two preparations. Briefly, our preparation involved column chromatography, first on silica gel columns. We had difficulty in obtaining clean separations of our active material from cortisone, so we turned to acetylation. Perhaps that was a hazardous procedure, inasmuch as Grundy, *et al.* (2), stated that acetylation of their material destroyed its activity. Of course, when one speaks of activity one should indicate the level at which it has been tested; we found a considerable amount after acetylation of a test portion of the material. Therefore, we decided to acetylate it.

Figure 1 summarizes one of our first columns. The fractions containing compounds A and B are indicated, and our activity is bracketed between the two vertical lines which include compound E. In accordance with the findings of Grundy, *et al.* (2), we also found that the activity traveled with much the same mobility as cortisone (Figure 2). After acetylation, however, we found that the sodium-retaining activity was much more mobile than cortisone acetate, and that we could achieve a clean separation of the latter. The zone containing the sodium-retaining activity also contained a

*Associates in this work were Drs. V. R. Mattox and A. Albert, of the Mayo Clinic, Rochester, Minnesota.

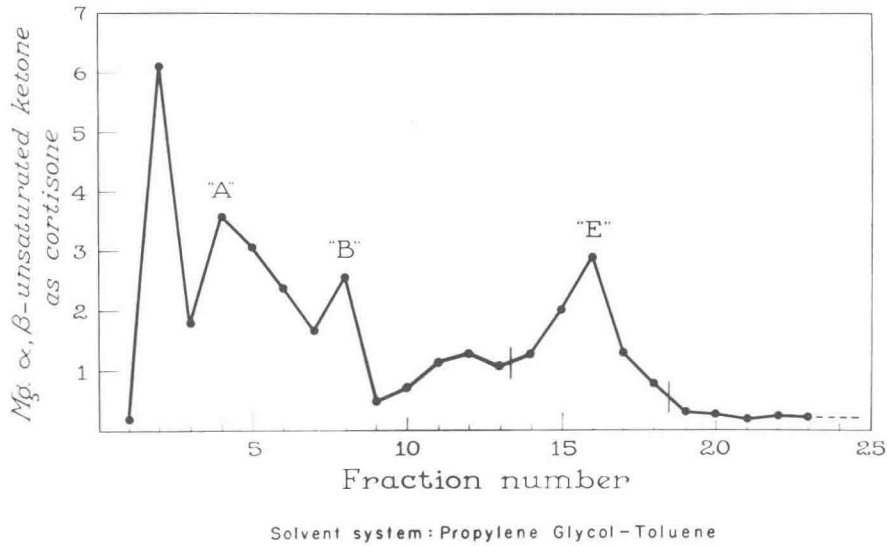

FIGURE 1. Fractionation of beef adrenal extract by column chromatography.

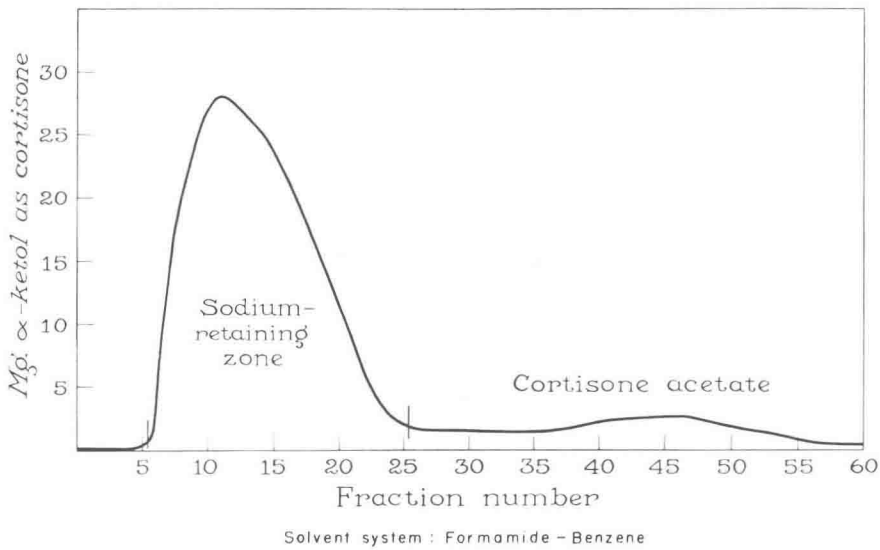

FIGURE 2. Fractionation of cortisone zone by column chromatography after acetylation.

number of other substances, some of which were crystalline, but the nature of which we do not know.

The acetate in our assay appeared to have about the same activity as desoxycorticosterone acetate (DCA), which of course was not very encouraging, but in view of the statement of Grundy, *et al.* (2), we thought we should hydrolyze it (Figure 3). The acetate

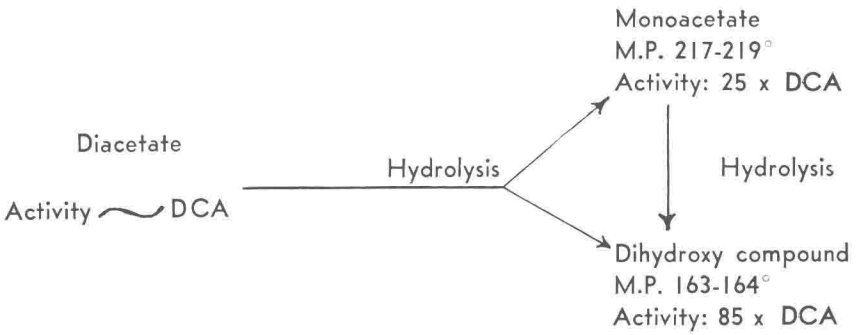

FIGURE 3. Enzymic hydrolysis of diacetate of sodium-retaining compound.

which we have designated, at least tentatively, as diacetate, was treated with citrus acetylesterase. After paper chromatography of the product of hydrolysis, we found there were two substances, one of which we called "monoacetate," and the other, the "dihydroxy compound." Those designations are tentative, but serve to identify the particular fractions.

The monoacetate crystallized first: it had an activity of approximately 25 times that of desoxycorticosterone acetate, which was encouraging in view of the low activity of the diacetate. Eventually we crystallized the dihydroxy compound, and found it had an activity of 85 or perhaps 100 times that of desoxycorticosterone acetate, which is comparable with the compound described by Simpson, Tait, Reichstein, *et al.* (3). Their compound has been described as having an activity of from 50 to 100 times that of DCA.

Figure 4 is a paper chromatogram, showing the mobilities of the three compounds just described, the diacetate, the monoacetate, and the free compound.

Figure 5 is a comparison of the free compound and the monoacetate with cortisone and cortisone acetate. You will note that the mobilities of cortisone and of the free compound are very similar, whereas the mobilities of the acetates are very different. As to the