

Arthur Bauman Clinical Symposium

Every Day Ethical Dilemmas for Thyroid Practitioners



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Disclosures

- PI for Abbvie diabetes study
- Consultant for Quest Diagnostics

The Discovery of the Radioimmunassay and Arthur Bauman, MD: Research Ethics and Omission of Attribution



Rosalyn Yalow

Born: 19 July 1921, New York, NY, USA

Died: 30 May 2011, New York, NY, USA

Affiliation at the time of the award: Veterans Administration Hospital, Bronx, NY, USA



Rosalyn Yalow – Nobel Prize Acceptance Speech

Radioimmunoassay: A probe for fine structure of biologic systems

December 7, 1977

Dr. I. Arthur Mirsky had hypothesized that maturity-onset diabetes might not be due to a deficiency of insulin secretion but rather to abnormally rapid degradation of insulin by hepatic insulinase.

To test this hypothesis we studied the metabolism of ^{131}I -labeled insulin following intravenous administration to non-diabetic and diabetic subjects.

We observed that radioactive insulin disappeared more slowly from the plasma of patients who had received insulin, either for the treatment of diabetes or as shock therapy for schizophrenia, than from the plasma of subjects never treated with insulin.

Rosalyn Yalow

Nobel Prize Acceptance Speech **Radioimmunoassay:**

A probe for fine structure of biologic systems December 7, 1977

We suspected that the retarded rate of insulin disappearance was due to binding of labeled insulin to antibodies which had developed in response to administration of exogenous insulin.

However classic immunologic techniques were not adequate for the detection of antibodies which we presumed were likely to be of such low concentration as to be non-precipitating. We therefore introduced radioisotopic methods of high sensitivity

Rosalyn Yalow Nobel Prize Acceptance Speech

Radioimmunoassay: A probe for fine structure of biologic systems

December 7, 1977

Using a variety of such systems we were able to demonstrate the ubiquitous presence of insulin-binding antibodies in insulin-treated subjects. This concept was not acceptable to the immunologists of the mid 1950's. The original paper describing these findings was rejected by Science and initially rejected by the Journal of Clinical Investigation.

A compromise with the editors eventually resulted in ***acceptance of the paper, but only after we omitted "insulin antibody" from the title*** and documented our conclusion that the binding globulin was indeed an antibody by showing how it met the definition of antibody given in a standard textbook of bacteriology and immunity.

THE JOURNAL OF CLINICAL INVESTIGATION

Published and Edited by The American Society For Clinical Investigation

622 WEST 168TH STREET
NEW YORK 32, NEW YORK

REJECTION LETTER

September 29, 1955

Dr. Solomon A. Berson
Radioisotope Service
Veterans Administration Hospital
130 West Kingsbridge Road
Bronx 68, New York

Dear Dr. Berson:

I regret that the revision of your paper entitled
"Insulin- I^{131} Metabolism in Human Subjects: Demonstration of
Insulin Transporting Antibody in the Circulation of Insulin
Treated Subjects" is not acceptable for publication in THE
JOURNAL OF CLINICAL INVESTIGATION. -----

----- The second major critic-
ism relates to the dogmatic conclusions set forth which are not
warranted by the data. The experts in this field have been
particularly emphatic in rejecting your positive statement that
the "conclusion that the globulin responsible for insulin bind-
ing is an acquired antibody appears to be inescapable". They
believe that you have not demonstrated an antigen-antibody re-
action on the basis of adequate criteria, nor that you have def-
initely proved that a globulin is responsible for insulin binding,
nor that insulin is an antigen. The data you present are indeed
suggestive but any more positive claim seems unjustifiable at
present.

Sincerely,



Stanley E. Bradley, M.D.
Editor-in-Chief

The Publication in JCI !

INSULIN-I¹³¹ METABOLISM IN HUMAN SUBJECTS:
DEMONSTRATION OF INSULIN BINDING GLOBULIN IN
THE CIRCULATION OF INSULIN TREATED SUBJECTS¹

By SOLOMON A. BERSON, ROSALYN S. YALOW, ARTHUR
BAUMAN,² MARCUS A. ROTHSCHILD,³ AND KATHARINA
NEWERLY

(From the Radioisotope Service, Veterans Administration
Hospital, Bronx, N. Y.)

(Submitted for publication August 22, 1955; accepted
October 17, 1955)

Earlier Publication in Journal of Clinical Investigation

DISTRIBUTION AND METABOLISM OF I¹⁸¹ LABELED
HUMAN SERUM ALBUMIN IN CONGESTIVE HEART
FAILURE WITH AND WITHOUT PROTEINURIA

BY ARTHUR BAUMAN,¹ MARCUS A. ROTHSCHILD,²
ROSALYN S. YALOW, AND SOLOMON A. BERSON

(From the Radioisotope Service, Veterans
Administration Hospital, Bronx, New York, N. Y.)

(Submitted for publication March 14, 1955; accepted
May 11, 1955)

Dr. Marcus Rothschild

interviewed by Dr. Adolf Friedman 2009
Clark Sawin Library of the Endocrine Society

I began working on blood volume, and then we got interested in albumin, and Arthur [Bauman] and I worked together. We worked with all the new radioactive material from Brookhaven in studying thyroid disease, and there was a chemist by the name of Kitty Newerly, and she would label the proteins and the insulin that we used and all the other stuff, and we started studying blood volume. We got interested in albumin.

Arthur came to me one day and he said, "Why don't we study some insulin?"

Dr. Marcus Rothschild

Clark Sawin Library

Years later, when they had kind of a celebration for Roz [Yalow] at the Plaza--along with a lot of famous people--Arthur got up and said, "I just want to tell everybody the idea to label insulin was Marc Rothschild's." I got up and said, "No, Arthur; it was yours."

Then there was dead silence because Roz [Yalow] was there and Sol [Berson] had died and, of course, she had won the Nobel Prize. So I always said it was Arthur's idea, and he always said it was my idea.

Marcus Rothschild- Clark Sawin Library

But anyway, we labeled some insulin; we gave it to patients-- there was no real way to get anyone to approve what we had done. We were going to give them a small amount of radioactive material, and we were going to draw some blood and study what happened to the material that we gave them. A lot of people said yes.

Sol [Berson] came in one day and he said, "What are you boys doing?" We showed him, and he went around a mental corner, which I never followed. Then we would spend the night there with him. He would play chess or the violin, and we would be trying to isolate the radioactive material from the plasma--went to the grocery store to get starch to build a starch block--and we built our own scintillation counters.

*And then he came in one day, and he dropped this paper on the desk and said, "**Boys, I hope you don't mind, I put my name first.**" We looked at each other, we read the paper, and I said, "You mean that's what we've been doing?" We "giggled" together, and he was wonderful. He was just the greatest man, greatest friend.*

Thyroid specific publication

Journal of Clinical Investigation

1956

THE EFFECT OF LARGE DOSES OF DESICCATED THYROID ON THE DISTRIBUTION AND METABOLISM OF ALBUMIN-I¹³¹ IN EUTHYROID SUBJECTS

BY MARCUS A. ROTHSCHILD,¹ ARTHUR BAUMAN,² ROSALYN S. YALOW, AND SOLOMON A. BERSON

(From the Radioisotope Service, Veterans Administration Hospital, Bronx 68, N. Y.)

(Submitted for publication August 3, 1956; accepted November 29, 1956)

My Conclusions

- While Roslyn Yalow credited Solomon Berson as her collaborator for the Nobel Prize,
- She never properly credited Dr. Arthur Bauman nor Dr. Marcus Rothschild.
- The Invention of the Radioimmunoassay is another story of research ethics and lack of proper attribution.
- I am delighted to moderate the Arthur Bauman Symposium and hope that we recognize Dr. Bauman's critical research contribution to medicine.

Arthur Bauman Symposium

- M. Sara Rosenthal, PhD
Director of Bioethics, University of Kentucky
The Limits of Autonomy in Thyroid Disease Management
- Peter Angelos, MD, PhD
University of Chicago
Associate Director, Maclean Center for Clinical Ethics
Ethical Issues in Robotic Transaxillary Surgery
- Keith Bible, MD, PhD
Mayo Clinic
Ethical Challenges with Tyrosine Kinase Inhibitors for Thyroid Cancer