Arthur Bauman Clinical Symposium
Every Day Ethical Dilemmas for Thyroid Practitioners

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PRESENTATION FROM THE 83rd ANNUAL MEETING OF THE AMERICAN THYROID ASSOCIATION, OCTOBER 16-20, 2013 (Loren Wissner Greene)
Loren Wissner Greene, MD, MA
Disclosures

• PI for Abbvie diabetes study
• Consultant for Quest Diagnostics
The Discovery of the Radioimmununassay 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
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.
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.
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.
Dr. Solomon A. Berson
Radioisotope Service
Veterans Administration Hospital
130 West Kingsbridge Road
Bronx 63, New York

Dear Dr. Berson:

I regret that the revision of your paper entitled "Insulin-\(^{131}\)I 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.

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The second major criticism 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 binding is an acquired antibody appears to be inescapable." They believe that you have not demonstrated an antigen-antibody reaction on the basis of adequate criteria, nor that you have definitely 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.

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Sincerely,

Stanley E. Bradley, M.D.
Editor-in-Chief
INSULIN-\textsuperscript{131} METABOLISM IN HUMAN SUBJECTS:
DEMONSTRATION OF INSULIN BINDING GLOBULIN IN
THE CIRCULATION OF INSULIN TREATED SUBJECTS\textsuperscript{1}

By SOLOMON A. BERSON, ROSALYN S. YALOW, ARTHUR
BAUMAN,\textsuperscript{2} MARCUS A. ROTHSCILD,\textsuperscript{3} AND KATHARINA
NEWERLY

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

(Submitted for publication August 22, 1955; accepted
October 17, 1955)
DISTRIBUTION AND METABOLISM OF I\(^{181}\) LABELED HUMAN SERUM ALBUMIN IN CONGESTIVE HEART FAILURE WITH AND WITHOUT PROTEINURIA

BY ARTHUR BAUMAN,\(^1\) MARCUS A. ROTHSCILD,\(^2\) 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)
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?”
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.
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.
THE EFFECT OF LARGE DOSES OF DESICCATED THYROID ON THE DISTRIBUTION AND METABOLISM OF ALBUMIN-$^{131}$ IN EUTHYROID SUBJECTS

BY MARCUS A. ROTHSCILD,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*