Radioimmunoassay and Related Methods: Introduction

Rosalyn S. Yalow, Ph. D.

Solomon A. Berson Research Laboratory,
Veterans Administration Medical Center, Bronx, New York

Department of Clinical Sciences, Montefiore Medical Center, Bronx, New York

INTRODUCTION

This is the 25th Anniversary of the first description of the measurement of plasma insulin in man using radioimmunoassay (RIA) (1). Within a few years following that report there was a burgeoning interest in the application of RIA for the measurement of peptidal hormones since the low concentrations of these substances in the unstimulated state (10^{-13}-10^{-10}M) required the remarkable sensitivity and specificity of RIA. However, it was not until a decade later that RIA was applied to the measurement of non-peptidal hormones as well as to medical specialties as diverse as pharmacology, infectious diseases and oncology.

It is noteworthy that soon after the description of RIA's for thyroxine, T_4, and triiodothyronine, T_3, by Chopra and associates in 1971 and 1972 (2,3), screening programs for neonatal hypothyroidism were initiated in several centers. The programs were based on the assay of T_4 and/or TSH extracted from a few drops of blood dried on filter paper (4-6). We now know that in the United States and many other areas of the world this disease occurs in about 1 in 4000 births but it has been shown to occur in 4% of the births in regions of endemic goiter (7). Early identification and treatment of this disease prevents needless mental retardation. Similar methodology can be applied to the early diagnosis of the congenital form of adrenogenital syndrome due to deficiencies of the 21-hydroxylase, 11-β-hydroxylase or 3-β-OH dehydrogenase enzymes although these diseases are less common than neonatal hypothyroidism.

The application of RIA to pharmacology was initiated by Parker and associates who in 1968 described the RIA for digitoxin (8). Within 5 years the method was extended to tens of drugs (9). Since then, RIA has had important application in the determination of circulating levels of drugs for which there is a very narrow range between efficacy and toxicity.

It was in 1970 that Walsh and associates (10) described the first RIA for an infectious agent – hepatitis B antigen, then known as Australia antigen. Within two years commercial kits became available which made practical the routine use of this assay for the testing of blood to be used for transfusion. RIA is now commonly applied in virology. In my Nobel lecture in 1977 I

predicted that RIA would soon revolutionize the diagnosis infectious diseases in areas other than in virology (11). Soon thereafter Straus and associates (12) described the first assay for a tuberculoprotein that offered the potential for permitting a rapid, inexpensive and safe assay for active tuberculosis. According to the World Health Organization there are currently 20 million people with active tuberculosis and the death rate attributable to this disease remains high – about 3 million a year. It is indeed fortunate for India that two physicians, Dr. Samuel from Bombay, and Dr. Kochupillai from Delhi, both of whom were trained in my laboratory, have undertaken to apply this methodology in a region where active tuberculosis remains a major public health problem. Dr. Ganatra, will describe in this session the studies carried on in his Bombay laboratory in this field. I look forward to the time when RIA and related methodologies will be applied to a variety of other bacterial, fungal, protozoan and helminthic pathogens that continue to afflict populations throughout the world.

The field of non-endocrine tumor markers was initiated by the work of Gold and associates in 1968 (13) who reported that the RIA of carcinoembryonic antigen (CEA) provided a sensitive and specific test for colonic and rectal cancer. Although CEA is now known to be insensitive with respect to early diagnosis of malignancy and is elevated in a variety of non-malignant conditions, it remains a very popular and widely used test. Since that time, the usefulness of several other tumor markers have been described. Dr. Irie will update us on the status of this work in Japan.

RIA opened a new field – currently called immunodiagnostics. For the most part the binding ligand is an antibody. However, the marker for the labeled antigen need not be a radioisotope. Enzyme and fluorescent dye markers have been employed quite successfully. They have proven to be most satisfactory for those substances present in relatively higher concentrations in blood or body fluids than are the peptide hormones. Dr. Miyai will update us on the comparison of RIA with the other marker assays.

The time for this session is much too short to do justice to all the material to be presented. We look forward to a series of very interesting papers.

REFERENCES

1) Yalow, R.S., and Berson, S.A.: Assay of plasma insulin in human subjects by immunological methods. Nature 184: 1648-1649, 1959.
2) Chopra, I.N.: A radioimmunoassay for measurement of thyroxine in unextracted serum. J. Clin. Endocrinol. Metab. 34: 938-947, 1972.
3) Chopra, I.J., Solomon. D.H. and Beall, G.N.: Radioimmunoassay for measurement of triiodothyronine in human serum. J. Clin. Invest. 50: 2033-2041, 1971.
4) Dussault, J.H., Coulombe, P. and Laberge, C.: Neonatal thyroid screening. In: Perinatal Thyroid Physiology and Disease, Fisher, D.A. and Burrow, G.N., eds., Raven Press, New York, p.221, 1975.
5) Larsen, P.R. and Broskin, K.: Thyroxine immunoassay using capillary blood samples collected on filter paper. In: Perinatal Thyroid Physiology and Disease, Fisher, D.A. and Burrow, G.N., eds. Raven Press, New York, p.231, 1975.
6) Walfish, P.G.: Screening for neonatal hypothyroidism using a dried capillary blood method: Observations on methodologic factors, selection criteria, and preliminary results. In: Perinatal Thyroid Physiology and Disease, Isher, D.A. and Burrow, G.N., eds. Raven Press, New York, p.239, 1975.
7) Jayaraman, K.S.: Goitre in India: Iodine prophylaxis falters. Nature 304: 205, 1983.
8) Oliver, G.C., Jr., Parker, B.M., Brasfield, D.L. and Parker, C.W.: The measurement of digitoxin in human serum by radioimmunoassay. J. Clin. Invest. 47: 1035-1042, 1968.
9) Spector, S.: Radioimmunoassay of drugs. In: Radioimmunoassay and Related Procedures in Medicine, Vol.II, International Atomic Energy Agency, Vienna, pp.233-248, 1974.
10) Walsh, J.H., Yalow, R.S. and Berson, S.A.: Detection of Australia antigen and antibody by means of radioimmunoassay techniques. J. Infect. Dis. 121: 550-554, 1970.
11) Yalow, R. S.: Radioimmunoassay: A probe for the fine structure of biologic systems. Science 200: 1236-1245, 1978.
12) Straus, E., Wu, N., Quraishi, M.A.H. and Levine, S.: Clinical applications of the radioimmunoassay of secretory tuberculoprotein. Proc. Natl. Acad. Sci. USA 78: 3214-3217, 1981.
13) Thompson, D.B.P., Krupey, J., Freedman, S.O. and Gold, P.: The radioimmunoassay of circulating carcinoembryonic antigen of the human digestive system. Proc. Natl. Acad. Sci. USA 64: 161-167, 1969.