NASA CONTRACTOR
REPORT

NASA CR-1395

NASA CR-1395

ANALYSES AND MEASUREMENTS OF BLOOD SAMPLES

by Eric Reiss

Prepared by
MICHAEL REESE HOSPITAL AND MEDICAL CENTER
Chicago, Ill.
for Ames Research Center

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION • WASHINGTON, D. C. • OCTOBER 1969

NASA CR-1395

ANALYSES AND MEASUREMENTS OF BLOOD SAMPLES

By Eric Reiss

Prepared under Contract No. NAS 2-4757 by
MICHAEL REESE HOSPITAL AND MEDICAL CENTER
Chicago, Ill.

for Ames Research Center

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION

For sale by the Clearinghouse for Federal Scientific and Technical Information
Springfield, Virginia 22151 – CFSTI price $3.00

FINAL REPORT ON CONTRACT NAS 2-4757
ANALYSES AND MEASUREMENTS OF BLOOD SAMPLES

A. SUMMARY AND RECOMMENDATIONS

This final report covers investigations accomplished during the effective period of the contract. Details of experimental procedures are given. We conclude on the basis of data now available, that the radioimmunoassay for parathyroid hormone (PTH) yields reliable and reproducible measurements in man and that the methods developed in our laboratory are applicable for the investigation of calcium metabolism during weightlessness in space flight. Despite substantial accomplishments, many problems remain. These problems are spelled out in detail. They emphasize the need for ongoing investigations and improvement in currently employed technics.

B. REPORT

I. The Assay Procedure

1. Production of Antibody: The original antibody was produced in a cockerel eight weeks of age at the time of the first injection. The antigen used for immunization was partially purified beef PTH, prepared from crude parathyroid gland powder (Wilson Laboratories) by the method of Rasmussen (J. Biol. Chem., 239:2852, 1964). This preparation had a biologic activity of 150 to 200 units per mg, as assayed by the Munson rat bio-assay procedure. The antigen was dissolved in saline and administered without adjuvant. Two intravenous injections of 40 mg each were given four weeks apart. One week after the second dose, 10 mg was injected intramuscularly on each of four consecutive days. Thereafter, 20 mg was injected intramuscularly at monthly intervals. The antibody was detected in maximal concentrations five months after the first injection.

A second antiserum was produced in a cockerel using the following immunization schedule: partially purified PTH was emulsified in complete Freund's adjuvant. The initial injection was 6 mg per chicken in the footpad. The same dose, preparation, and route of injection were repeated 10 days later. Thereafter, monthly booster doses of 20 mg per chicken were given intramuscularly, the antigen being again suspended in Freund's adjuvant. A usable antibody was detected six months after the initial injection. This animal is still alive. Although the antibody has not been studied as completely as the original one, sufficient experience has been gained to show that it possesses high affinity for both bovine and human PTH. Its affinity for hormone, however, is not as strong as that of the originally produced antibody.

2. Purified Antigen: Highly purified bovine hormone was prepared on large columns of sephadex G-100 (Endocrinology, 75:291, 1964; J. Biol. Chem., 239: 2852, 1964). The biologically active peaks were cycled through sephadex a second time in order to afford better separation. The final product gave a single band on starch gel electrophoresis and was assayed at a biologic potency of 1800-2000 units per mg. Recently, scientists working at the Wilson Laboratories have produced an excellent highly purified preparation of bovine PTH. The Wilson scientists had the benefit of consultations with Drs. Gerald Aurbach and John Potts. Their preparation was further purified by passage through carboxymethylcellulose (Recent Progr. in Hormone Res., 22:101, 1966). Experience with this excellent preparation gave results that were indistinguishable from those

obtained with the product prepared by us.

3. Labelling of the Antigen: Highly purified PTH was labelled by the method of Greenwood and Hunter (Biochem. J., 89:114, 1963). Four µg of highly purified PTH is labelled with 3 mc of Iodine-131, which is supplied in minimal volume. All solutions are made in 0.05 M phosphate buffer, pH 7.5. Twenty-five µl of 0.5 M phosphate buffer, pH 7.5, is added to the Iodine-131. Next, 25 µl containing 4 µg of hormone is added. One hundred µg of chloramine T suspended in 25 µl is next added to the mixture and allowed to react with gentle agitation for a period of 30 seconds. Immediately thereafter, 0.25 mg of sodium metabisulfite suspended in 0.1 ml is added, and the reaction mixture is agitated gently for approximately 15 seconds. The next addition is 0.2 ml of a 1 per cent solution of potassium iodide. The reaction mixture is then transferred to a tube containing 1 ml of normal human serum. The reaction vial is rinsed with 0.2 ml of potassium iodide and the wash is added to the tube containing the serum.

For effective labelling, the source of Iodine-131 appears to be critical. We have had experience with several suppliers. The most consistently satisfactory results have been obtained with Iodine-131 secured from the Isoserve Division of Nuclear Cambridge, which supplies the isotope in small conical plastic containers. In most labelling procedures, a specific activity of around 500 mc per mg is achieved. However, there are occasions when the iodinization procedure fails. Whether this is related to some defect in the isotope or in the labelling procedure is not known. All laboratories engaged in labelling of peptide hormones have experienced the same difficulty.

4. Purification of Iodinated PTH: Absorption of the reaction mixture on silica gel has proved simple and useful in our experience (Nature, 212:375, 1966). The details as practiced in our laboratory are as follows: five mg of Quso G-32 (Philadelphia Quartz Company) is added to the reaction mixture and shaken briefly. After centrifuging at 3000 r.p.m. for five minutes, the supernatant is decanted and discarded. The Quso is then washed once with 2 ml of distilled water. After centrifugation, the wash is discarded. Purified labelled PTH is eluted from the Quso by agitation with 0.5 ml of 20 per cent acetone in 1 per cent acetic acid. After the addition of 1.5 ml of distilled water and centrifugation the supernate is collected and the Quso is discarded. A second centrifugation is then performed to insure removal of all the Quso. The material is evaporated to one half dryness by lyophilization and resuspended in 1 ml of 0.1 per cent acetic acid.

On electrophoresis, approximately 90 to 95 per cent of the radioactive PTH prepared by this procedure adheres to the point of application. However, recent experience has shown that the silica gel procedure fails to remove substantial amounts of free Iodine-131. This failure to remove free iodide completely does not interfere with the assay when bound and free hormone are separated by any means involving an electric current. Free Iodine-131 does appear to lessen sensitivity when separation is accomplished chromatographically and probably also with the use of charcoal methods. Our information on the latter point is not yet complete, as discussed below.

5. The Incubations: All dilutions of antisera, test sera, labelled PTH, and unlabelled PTH were made in barbital buffer, pH 8.6, ionic strength 0.05, containing 1 per cent bovine serum albumin. One-tenth ml of a 1:1000 dilution

of antiserum was mixed with an equal volume of buffer containing various quantities of test sera or unlabelled highly purified bovine PTH and incubated at 4°C for 96 hours. One-tenth ml of labelled PTH was then added, and the incubation was continued for another 48 hours. The final dilution of antiserum was 1:3000. One-tenth ml of a 1:1000 dilution of normal chicken serum was incubated with labelled PTH as a control. The labelled PTH was diluted so as to yield roughly 75,000 counts per minute per .1 ml on an autogamma counter (Nuclear Chicago) with a counting efficiency for Iodine-131 of approximately 45 per cent.

6. Separation of Antibody Bound and Free Hormone: This was accomplished by electrophoresis on cellulose acetate, 34 volts per cm for 12 minutes at room temperature in an EDTA-Tris-Borate buffer, pH 8.6. The procedure gave a reproducible 2 cm distance between bound and free hormone as indicated by scanning. The radioactivity adhering to the point of application was interpreted as representing free hormone. The electrophoretic strips were cut into segments containing free and protein-bound hormone and counted in an autogamma counter for a sufficient period to yield a counting error of less than 1 per cent.

With this last procedure, 3 to 12 per cent of the labelled PTH migrated electrophoretically with the serum proteins of normal chicken sera. This was interpreted as representing either incubation damage or incomplete purification of labelled PTH after the labelling procedure. Addition of up to 20 µl of hypoparathyroid serum to the mixture does not appreciably increase the fraction of incubation damage. For each experiment, the percentage of total radioactivity in the protein fraction of normal chicken sera controls was determined and subtracted from the protein-bound radioactivity of test samples.

Three points are noteworthy about this procedure. First, the dilution of antibody was such as to yield a bound to free hormone ratio of approximately 1 in the absence of unlabelled PTH in the incubation mixtures. Secondly, the extraordinary sensitivity of the assay procedure is indicated by the ready detection of PTH in normal human sera when these sera were diluted 1:30 in the final incubation mixture. In hyperparathyroid sera, 1:300 dilutions of test sera in the incubation mixture gave readily detectable measurements. Thirdly, the inefficiency of the procedure is readily apparent. Since only small quantities of the incubation mixture can be applied to the cellulose acetate strips (5-8 µl), an inordinately large amount of labelled hormone has to be added to the incubations in order to yield measureable radioactivity after separation of bound and free hormone. The consequences of this inefficiency are discussed below.

7. Assay Samples: All analyses are performed on serum. It has been found that heparin definitely interferes with the assay. Preliminary results suggest that EDTA does not interfere, but this information is preliminary. Serum is therefore the preferable specimen. Ten ml of whole blood is drawn. The clot is allowed to retract in the refrigerator. After centrifuging, the serum is separated and frozen promptly. If samples are sent, they should be packaged in dry ice. The minimal amount of serum required for the assay of normal sera is 0.3 ml of serum. However, to permit duplicate analyses, a larger amount of serum is preferable. Repeated analyses of the same serum yield a coefficient of variation of nine per cent.

II. VALIDATION

Although the extraordinary sensitivity of radioimmunoassays is well established by experience, there are difficulties in validating the procedures in biologic terma. The possibility always exists that there may be some dissociation between immunologic and biologic activity. For PTH, in fact, data have been published to indicate that the biologically and immunologically active portions of the molecule are not identical (Recent Progr. in Hormone Res., 22:101, 1966). In man, the best validation of a radioimmunoassay procedure is obtained by clinico-pathologic correlations (Adv. in Int. Med., 13:183, 1967).

1. Normal Sera: When radioimmunoassays are first developed, it is commonly experienced that measurements are obtainable when the serum concentration is high but not when it is normal. The assay as developed in our laboratory permits ready measurement of normal concentrations of PTH at high dilutions of test sera. In the only published series other than our own (Science, 154:907, 1966), PTH was undetectable in many normal sera. In six hypoparathyroid sera tested so far, serum PTH was unmeasureable. This represents essential data for specificity.

Results obtained with 46 normal subjects are shown in Figure 1. The units of measurement are arbitrary, relating the potency of test sera to that of an arbitrarily selected extended hyperparathyroid serum. The mean normal value was 31 with a standard deviation of 14.

2. Hyperparathyroid Sera: The specificity of radioimmunoassay of PTH has been seriously questioned by the report of others that hyperparathyroid sera frequently yield PTH measurements in the normal range (Science, 154:907, 1966). No overlap has been observed between normal and hyperparathyroid sera in our experience with 63 patients with primary hyperparathyroidism. This is a critical argument in favor of the specificity of our assay procedure (Proc. Soc. Exp. Biol. Med., 128:501, 1968). Further evidence of specificity was obtained by serial measurements of serum PTH before, during, and after surgical removal of parathyroid adenomas. The sequential decline from high serum PTH to normal levels within five to twelve hours after the operation has been documented repeatedly.

Relevant clinical data, source of material, pathologic findings, and results of the PTH assay are shown for all 63 patients in Table I. Of the 63 patients studied, 26 were derived from Michael Reese Hospital and Medical Center. The remainder were referred from various other centers. The mean PTH value for the entire group was 384; the standard deviation was 191. It should be noted that the standard deviation is not an appropriate measure of dispersion for these data. A more meaningful parameter, the median, was 350. It is especially noteworthy that we encountered no overlap between normal and hyperparathyroid sera. The present extended series includes data previously published before initiation of this contract (Proc. Soc. Exp. Biol. Med., 128:501, 1968).

In Figure 2 are shown the detailed values of PTH before, during, and after removal of parathyroid adenomas. In Table II are shown the PTH data before and 24 hours after surgery for removal of a parathyroid adenoma.

3. Other Clinical States: Because of our recent efforts to improve the methodology, little additional information has been gained since submission of the report ending the period September 30, 1968. Of importance to the contract is a recent inquiry from Dr. Stephen Hulley of the PHS Hospital in San Francisco. After earlier consultation with us, he has systematically collected samples from human volunteers subjected to systematic immobilization. The immobilization studies have apparently been carried out very carefully. The balances of calcium, phosphorus, and nitrogen were measured. If immobilization results in changes of serum PTH, this study should provide useful and definitive evidence.

III. PROBLEMS

1. Limitations of the Assay: It is clear from the description of the assay as developed in our laboratory that it is slow and inefficient. There is every reason to believe that the sensitivity could be further increased if the amount of labelled PTH in the incubation mixtures could be reduced. The present procedure also has the limitation of being wasteful of antibody. Although the current supply of antibody is sufficient for the conduct of these and other studies, the supply is limited and should not be wasted.

2. The Critical Nature of the Assay System: During the past three months, several attempts have been made to improve efficiency. A double antibody technic was explored. This procedure, based on the precipitation of antigen-antibody complexes by an anti-chicken gamma globulin, yielded reproducible results. However, the procedure resulted in loss rather than gain in sensitivity and was therefore rejected. We next investigated a chromatographic technic of separation on a 3 MC paper. Although this procedure permitted the use of higher dilutions of antibody, loss of sensitivity was again encountered.

The most promising procedure appears to be the dextran-coated charcoal method of Herbert (J. Clin. Endocrinology Met., 25:1375, 1965). It has been used successfully for the assay of PTH by Drs. Claude Arnaud, John Potts, and Jeffrey O'Riordan. We have been in touch with these groups and have exchanged antisera as well as technical information. The procedure for separating antibody-bound and free hormone critically determines the dilution of antibody to be used and the amount of labelled hormone required for optimal sensitivity. Unless each procedure is carefully standardized in a particular laboratory, misleading information is obtained. For example, our best antiserum, which has proved high affinity for human PTH, did not give good results in Dr. O'Riordan's laboratory when tested by the charcoal procedure against partially purified human PTH. The reason for this discrepancy of results is that Dr. O'Riordan used an antibody dilution that was appropriate for our system of separation but not for his. As a result, he appears to have had marked antibody excess, which prevented displacement of labelled hormone.

The available data leave no doubt that these problems are soluble. Improvement in the efficiency of the system, more abundant availability of antibody, and better comparability of results obtained in various laboratories would be highly desirable.

3. PTH in Species Other than Man: Valuable data have been published by others on the physiologic variation of PTH in the cow and the goat. We have had

some experience in attempting to measure PTH in the dog. It is apparent that dog PTH reacts with our antibody with much less affinity than bovine or human PTH. However, dog PTH is measureable, albeit at a lower sensitivity. Our experience with rat PTH is very limited. The preliminary data show that measuring rat PTH with currently available antisera will be exceedingly difficult. We have had no experience with simian PTH.

4. Heterogeneity of Parathyroid Peptides: It has been reported (J. Clin. Endocr., 28:1037, 1968) that in various pathologic conditions in man several immunologically distinct peptides are secreted by the parathyroid glands. This important observation has not been confirmed in other laboratories. It would be important for another group of investigators to validate these observations. Although the question of heterogeneity is of general scientific interest, it is not likely to be of immediate concern to the objectives of this contract since increased levels of serum PTH during space flight would be derived from normal rather than pathologic parathyroid tissue.

5. The Half-Life of PTH: A large body of data has been accumulated on the half-life of PTH in the cow (Endocrinology, 83:1043, 1968). When parathyroid function is suppressed by the infusion of calcium, plasma PTH in the cow disappears with an apparent half-life of approximately 20 minutes. Similar experiments performed by us in man yield a half-life of approximately three hours both in normal subjects and in patients with secondary hyperparathyroidism. The reason for the discrepance of results in the two species is not apparent.

Results of calcium infusions in three normal subjects are shown in Figure 3. In these experiments, calcium was infused in the form of calcium gluconate-glucoheptinate for a period of four to eight hours at a rate of 4 mg of calcium per kg per hour. In normal subjects, serum PTH was normal at the beginning of infusion and decreased sequentially with an apparent half-time of hormone disappearance of three hours. A similar rate of hormone disappearance was measured in patients with secondary hyperparathyroidism. An example of this is shown in Figure 4 for a patient with mild renal insufficiency.

TABLE I

MICHAEL REESE HOSPITAL PATIENTS

NO.	PATIENT	SIGNS AND SYMPTOMS	Ca 9.5-10.5 mg/100 ml	P 2.5-4.00 mg/100 ml	PTH*	PATHOLOGIC FINDINGS
1.	D.H.	Giant cell tumor in roof of mouth	11.-12.5	3.3	425	Adenoma - 1.6 g
2.	B.H.	Repeated renal calculi; Anxiety	9.5-11.3	2.4-3.2	190	Hyperplasia
3.	S.G.R.	Mild hypertension; Repeated renal calculi	9.0-10.4	2.9-3.3	230	Adenoma - 0.875 g
4.	S.K.	None given	11.1-12.4	2.2	211	Adenoma
5.	E.F.	Slight bone demineralization	11.2-13.4	2.4-2.6	420	Adenoma - 2.2 g
6.	A.R.	Headaches, shoulder pain; repeated renal calculi; anxiety	9.8-12.0	2.2-3.0	307	Adenoma - 2 mm diam.
7.	E.T.	Repeated renal calculi; joint pain	10.7-12.0	2.7-3.2	215	Hyperplasia
8.	J.T.	Mild hypertension; Anxiety, weakness	10.0-12.0	2.4-4.4	200	Adenoma 2.5 x 1 cm.
9.	E.B.	Hypertension	10.8-12.4	Normal	357	Adenoma
10.	R.B.	Joint and back pain; Slight demineralization of spine	11.0-12.5	1.5-4.0	259	Adenoma - 0.5 g
11.	L.L.	Hypertension; headaches; Joint pain	10.2-11.0	2.2-3.3	400	Adenoma
12.	K.S.	Repeated renal calculi; Bone demineralization	12.3	2.8	555	Adenoma
13.	O.C.	Renal Colic	10.5-11.8	3.1	225	Adenoma - 0.5 g
14.	J.W.	Shoulder pain; Headaches; weakness	10.6-10.7	2.9-3.1	650	Hyperplasia
15.	I.W.	Asymptomatic	11-13.0	2.5-3.6	575	Adenoma 2.5 x 1 cm.
16.	L.J.	Asymptomatic	10.5-11.0	3.1	150	Hyperplasia
17.	M.S.	None given	9.8-11.5	2.4-3.9	100	Adenoma
18.	R.C.	Hematuria; Renal calculus	11.-11.8	2.6-3.4	260	Adenoma

* Parathyroid Hormone

(Continued)

TABLE I (Continued)

NO.	PATIENT	SIGNS AND SYMPTOMS	mg/100 ml	mg/100 ml	PTH*	PATHOLOGIC FINDINGS
19.	D.D.	Severe Bone Demineralization	9.2-9.5	2.0-3.6	720	Adenoma - 8.7 g
20.	R.Mc	Mild hypertension; Fatigue	10.9-13.4	-	400	Adenoma - 1.5 g
21.	B.G.	Fatigue; Family history; Mild hypertension	9.5-10.9	1.0-2.8	350	Hyperplasia
22.	M.D.	None given	10.0-12.2	2.2-3.5	185	Adenoma
23.	L.P.	Renal calculi	11.5-12.0	2.0-3.0	282	Adenoma - 1.38 g
24.	G.M.	Asymptomatic	11.7-12.1	2.5-2.8	348	Adenoma - 2.5 cm.
25.	A.P.	Diabetes-	9.8-10.9	-	350	Adenoma
26.	E.	Severe bone disease	12.0	3.0	561	Hyperplasia

* Parathyroid Hormone

(Continued)

TABLE I (Continued)

-3-

PATIENTS FROM OTHER MEDICAL CENTERS

NO.	PATIENT	SOURCE	PTH*	PATHOLOGIC FINDINGS
27.	M.H.	Dr. H. Rasmussen (Univ. of Pennsylvania)	255	Hyperplasia
28.	A.N.	Dr. J. A. Colwell (V.A. Research Hosp.,Chicago)	367	Adenoma
29.	M.W.	" " " "	300	Adenoma
30.	F.G.	Dr. G. Perkoff (Wash. U. St. Louis, Mo.)	434	Hyperplasia
31.	(1)	Dr. L. Avioli (Washington Univ., St. Louis)	455	Adenoma
32.	(2)	" " " "	380	Adenoma
33.	(3)	" " " "	300	Adenoma
34.	(4)	" " " "	565	Adenoma
35.	(5)	" " " "	225	Adenoma
36.	M.W.	Dr. Edward Paloyan (Univ. of Chicago)	700	Adenoma
37.	E.W.	" " "	400	Adenoma
38.	I.C.	" " "	525	Adenoma
39.	W.G.	" " "	480	Adenoma
40.	J.S.	" " "	525	Adenoma
41.	L.K.	" " "	700	Adenoma
42.	J.H.	" " " (Recurrent hyperparathyroidism)	1000	Multiple adenomas
43.	F.	Dr. Edward Paloyan (Univ. of Chicago)	250	Adenoma
44.	O.J.	" " "	625	Adenoma
45.	E.W.	" " "	225	Adenoma
46.	D.W.	" " "	480	Hyperplasia
47.	D.D.	" " "	300	Adenoma

* Parathyroid Hormone

(Continued)

TABLE I (Continued)

NO.	PATIENT	SOURCE	PTH*	PATHOLOGIC FINDINGS
48.	R.R.	Dr. Jack Pickleman (Univ. of Chicago)	390	Hyperplasia
49.	M.F.	" " "	195	Adenoma
50.	R.T.	" " "	348	Adenoma
51.	R.L.	" " "	478	Adenoma
52.	A.Mc.	" " "	257	Adenoma
53.	A.J.	Dr. R. Utiger (Washington Univ., St. Louis)	125	Adenoma
54.	Z.L.	Dr. Herta Spencer (West Side V.A. Hospital, Chicago, Illinois)	179	Adenoma
55.	E.T.	Dr. R. H. Egdahl (Massachusetts Memorial Hospital)	600	Adenoma
56.	A.N.	" " "	1000	Hyperplasia
57.	G.E.	" " "	345	Adenoma
58.	R.J.	" " "	592	Adenoma
59.	A.G.	" " "	338	Hyperplasia
60.	L.F.	" " "	225	Adenoma
61.	S.	" " "	364	Adenoma
62.	D.G.	" " "	109	Adenoma
63.	L. Mc.	" " "	260	Adenoma

* Parathyroid Hormone

TABLE II

NO.	PATIENT	PRE-OP PTH	POST-OP PTH
1.	I.W.	575	23
2.	R.C.	260	40
3.	R.Mc.	400	31
4.	D.H.	425	51
5.	B.H.	190	15
6.	J.T.	200	26
7.	E.T.	600	41
8.	H.F.	730	32
9.	A.W.	1000	52
10.	G.E.	345	11
11.	R.J.	592	24
12.	L.F.	225	39
13.	A.G.	338	49
14.	A.R.	300	35
15.	J.W.	650	60
16.	L.	1570	71
17.	B.G.	390	47
18.	S.G.R.	266	64
19.	E.F.	420	54
20.	H.Q.	510	12.2

DISTRIBUTION OF PTH IN NORMAL SUBJECTS

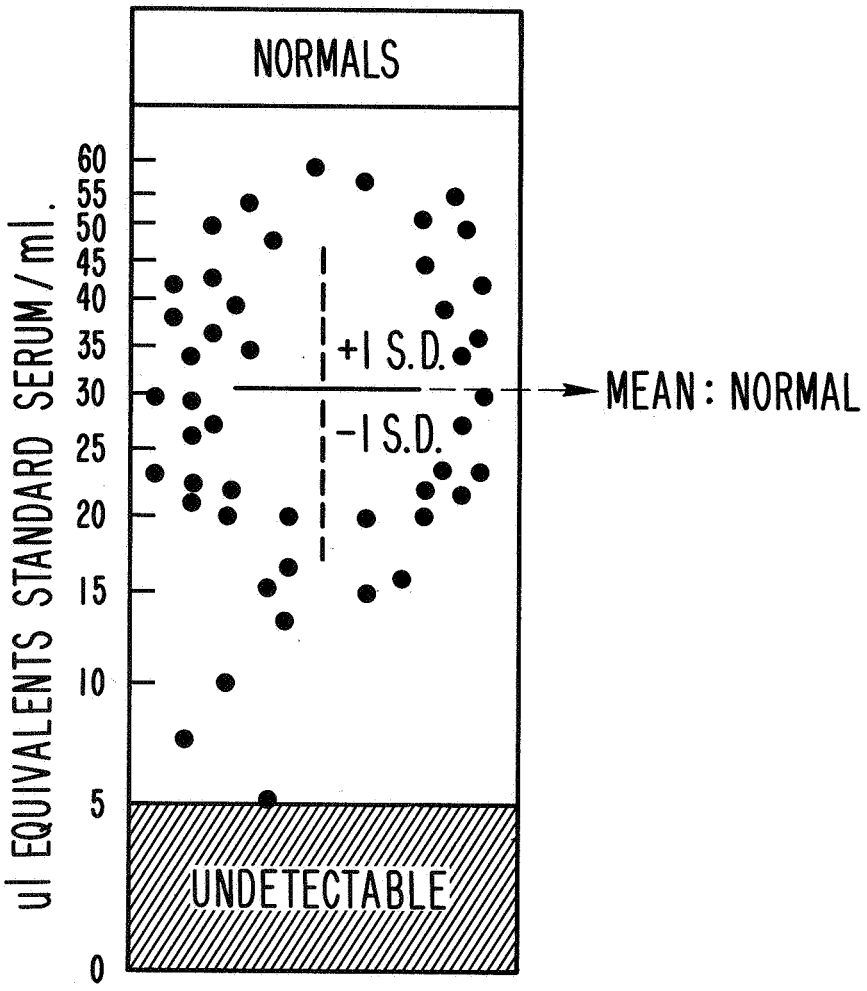
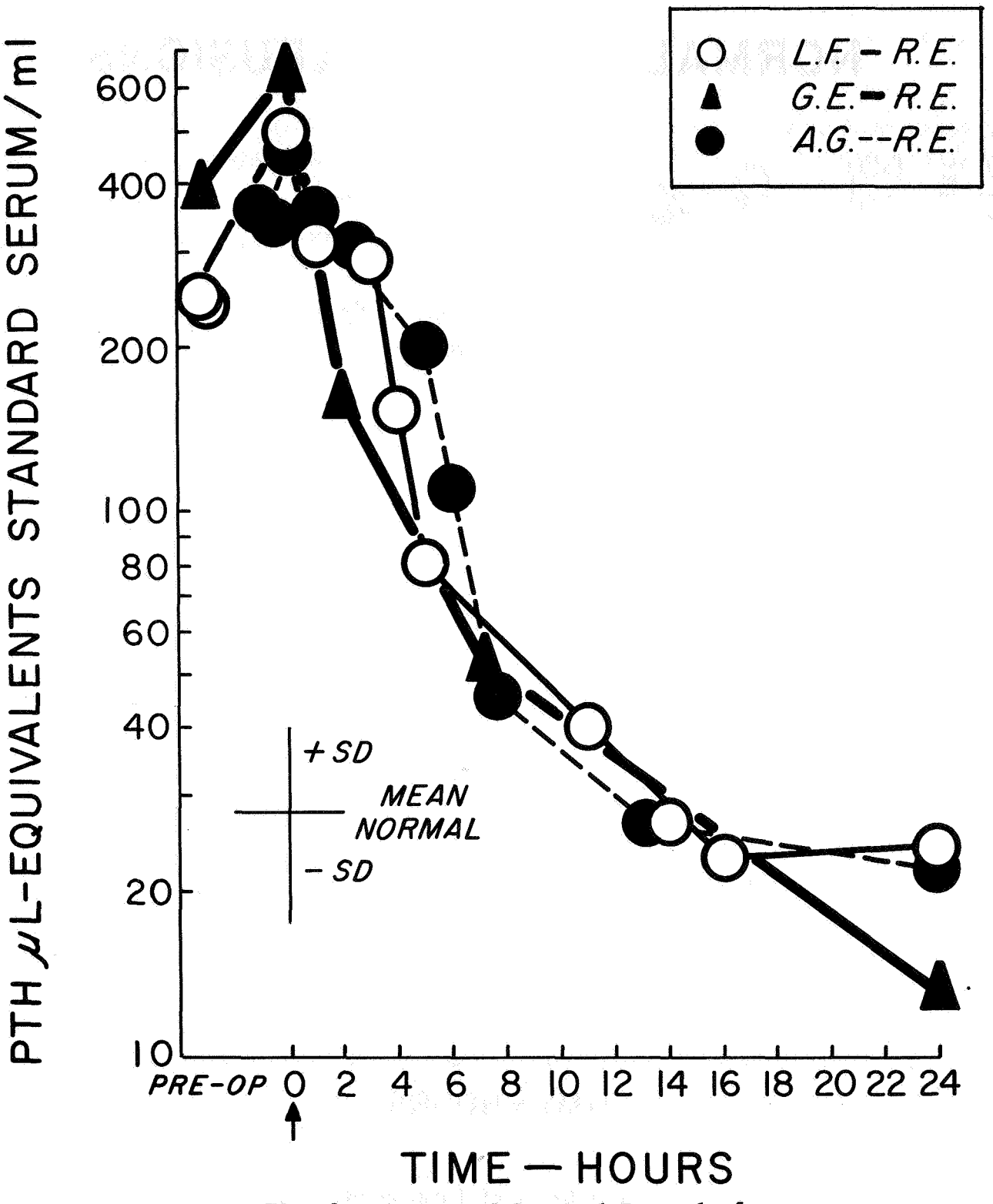
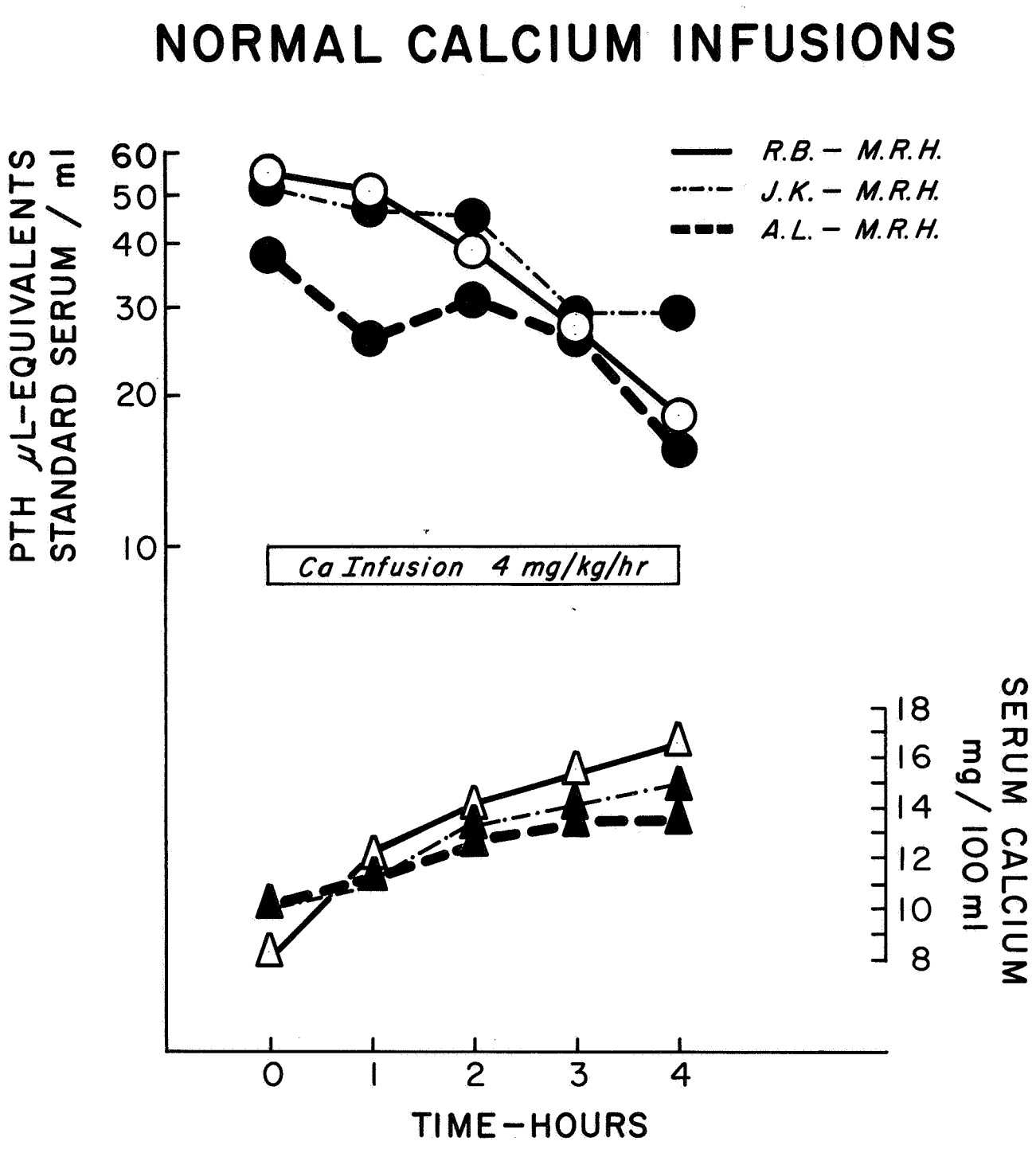


FIGURE 1



-Fig. 2- Effect of Surgical Removal of Parathyroid Adenomas on Level of Blood Parathyroid Hormone



-Fig. 3- Effect of Calcium Infusion on the Level of Parathyroid Hormone in Normal Subjects

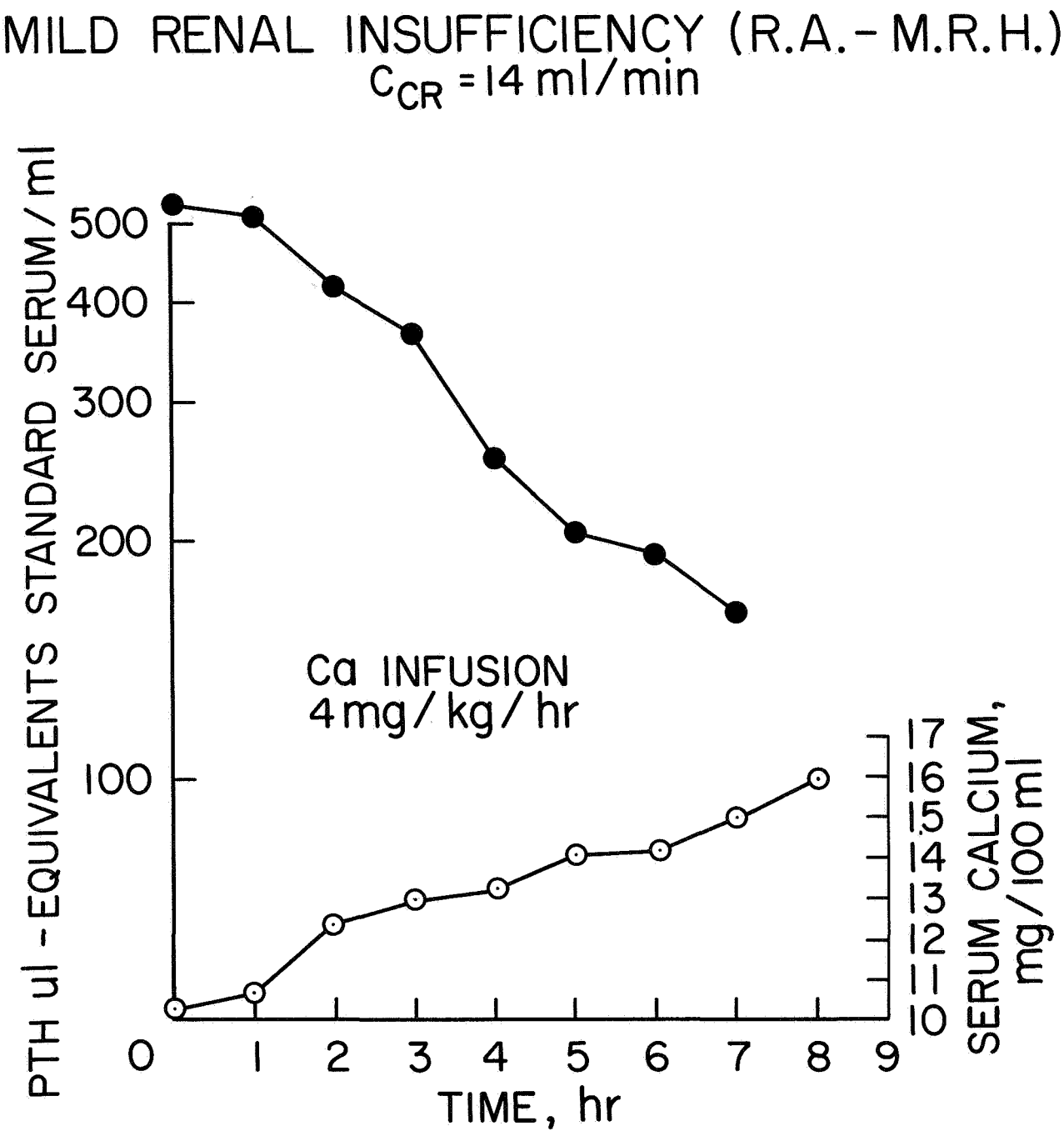

MILD RENAL INSUFFICIENCY (R.A.- M.R.H.)
C_{CR} = 14 ml/min
PTH ul-EQUIVALENTS STANDARD SERUM/ml
500
400
300
200
100
Ca INFUSION
4 mg/kg/hr
0
1
2
3
4
5
6
7
8
9
TIME, hr
17
16
15
14
13
12
11
10
SERUM CALCIUM, mg/100 ml

FIGURE 4

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION
WASHINGTON, D.C. 20546

OFFICIAL BUSINESS

FIRST CLASS MAIL

POSTAGE AND FEES PAID
NATIONAL AERONAUTICS AN
SPACE ADMINISTRATION

POSTMASTER: If Undeliverable (Section 158 Postal Manual) Do Not Return

"The aeronautical and space activities of the United States shall be conducted so as to contribute . . . to the expansion of human knowledge of phenomena in the atmosphere and space. The Administration shall provide for the widest practicable and appropriate dissemination of information concerning its activities and the results thereof."

—NATIONAL AERONAUTICS AND SPACE ACT OF 1958

NASA SCIENTIFIC AND TECHNICAL PUBLICATIONS

TECHNICAL REPORTS: Scientific and technical information considered important, complete, and a lasting contribution to existing knowledge.

TECHNICAL NOTES: Information less broad in scope but nevertheless of importance as a contribution to existing knowledge.

TECHNICAL MEMORANDUMS: Information receiving limited distribution because of preliminary data, security classification, or other reasons.

CONTRACTOR REPORTS: Scientific and technical information generated under a NASA contract or grant and considered an important contribution to existing knowledge.

TECHNICAL TRANSLATIONS: Information published in a foreign language considered to merit NASA distribution in English.

SPECIAL PUBLICATIONS: Information derived from or of value to NASA activities. Publications include conference proceedings, monographs, data compilations, handbooks, sourcebooks, and special bibliographies.

TECHNOLOGY UTILIZATION PUBLICATIONS: Information on technology used by NASA that may be of particular interest in commercial and other non-aerospace applications. Publications include Tech Briefs, Technology Utilization Reports and Notes, and Technology Surveys.

Details on the availability of these publications may be obtained from:

SCIENTIFIC AND TECHNICAL INFORMATION DIVISION

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION

Washington, D.C. 20546