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ORGAN AND TISSUE RADIOACTIVITY FOLLOWING PARENTERAL ADMINISTRATION OF

CO⁶⁰ VITAMIN B₁₂ *#

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Vitamin B₁₂ is found in practically all animal tissues and products, and the concentrations cover a wide range. In ruminants the vitamin is synthesized by micro-organisms in the forestomach, provided adequate cobalt is available. In humans and higher animals the content in tissues and blood is dependent on dietary intake. Regardless of source, the vitamin is carried by the blood stream to all parts of the body and taken up and bound by the tissues with varying avidity. In animal products the maximal amount of vitamin B₁₂ is found in beef liver. (16) Kidney and heart contain about one-half of this value. Fish meal and fish solubles also contain a considerable amount of vitamin B₁₂.

In 1950 Couch and Olcese reported that liver, kidney and spleen are the main storage organs of vitamin B₁₂ in chicks. (4) Barbee and Johnson studied the distribution of radioactivity following oral and parenteral administration of the labeled vitamins to rats. (2) Twenty-two hours after ingestion 92% of activity was present in the feces. After intramuscular injection 95% was excreted in the urine in the same period of time. In 1952 Rosenblum and co-workers showed that following parenteral administration of Co⁶⁰ vitamin B₁₂ to rats, the highest activity was found in kidneys, muscle, liver, skin and intestinal tract, in the order named. (15) They also found some activity in testes, blood heart, brain, spleen and bone marrow. Miller and co-workers reported that following injection of 1.0 µg of Co⁶⁰ vitamin B₁₂ to guinea pigs and hamsters, the liver was the main organ of storage. (12) The main route of excretion was in the urine. They corroborated previously reported findings that in the rat the highest concentration of radioactive vitamin B₁₂ was in the kidney.

In 1956 Meyer and co-workers studied the distribution of vitamin B₁₂

by means of surface body counting following intramuscular injection of Co^{60} vitamin B_{12} into human subjects. Maximal radioactivity was found over liver, spleen and kidney, in the order named, and was recorded over the liver up to 315 days after injection. (11) Sevensen reported the average vitamin B_{12} content of liver was $0.72 \mu\text{g}$ per gram of wet tissue. (17) In cirrhosis these values were reduced to $0.26 \mu\text{g}$ per gram, and in two cases of pernicious anemia the content was less than $0.1 \mu\text{g}$ per gram. Doscherholmen and Hagen reported that radioactive vitamin B_{12} stored in liver is extremely resistant to flushing out with non-radioactive material. (6) They administered 100 doses of 1.0 mg each during seven months and found that radioactivity measured over the liver was 20% of the initial value.

In 1959 Halstead and his group reported on vitamin B_{12} content of various organs and tissues obtained at autopsy. (9) The highest values were $0.614 \mu\text{g}$ per gram of normal liver and $0.263 \mu\text{g}$ per gram in the cirrhotic patient. The next highest values were $0.103 \mu\text{g}$ per gram in kidney and $0.41 \mu\text{g}$ per gram in spleen. Cooperman and co-workers reported the distribution of radioactivity after five daily injections of $0.135 \mu\text{g}$ of Co^{60} vitamin B_{12} to dogs. (3) After 14 days they found distribution of radioactivity after tracer doses closely paralleled total vitamin B_{12} content of viscera. Liver contained the most vitamin B_{12} because of its size. The gastrointestinal tract was next with more than half in the stomach. In brain the cerebrum had ten times as much activity as other areas, with greatest concentration in the corpus callosum. The pituitary gland had the highest activity per gram of tissue. Next in order were kidney and pancreas, each of which had a greater concentration than liver.

In 1960 and 1961, Doscherholmen, Finley and Hagen reported on autopsies performed on 11 subjects, two hours to 133 days after oral administration of 0.56 μg of Co^{60} vitamin B_{12} plus intrinsic factor.(7,8) A summary of autopsy findings shows that up to 7 hours after ingestion of labeled doses virtually all of the visceral radioactivity was in the wall of the small intestines. After 24 hours radioactivity of small bowel dropped to 30%, and after 42 hours to 28% of total visceral content. Between 85 and 309 hours after ingestion of labeled B_{12} radioactivity was between 5 and 13%, and in two subjects who died 13 and 113 days later, only 1 to 2% were found in the intestinal wall. After 24 hours approximately 55% of administered dose was in liver and the remainder was in spleen, kidneys, pancreas, lungs and heart. Spleen and kidneys reached maximal values earlier than those in liver, and also showed a more rapid decline. The biological half-life for vitamin B_{12} in liver was found to be approximately one year. In 1961 Adams reported on radioactivity of liver in 17 patients who survived 24 hours to 56 days after intravenous administration of 0.5 to 4.0 μg of radioactive vitamin B_{12} .(1) There was considerable variation of organ radioactivity, ranging from 29 to 62% of administered dose. These variations were irregularly spaced and could not be related to time of death after administration of the vitamin. Most of the vitamin was in liver and relatively little in organs other than spleen, lungs and kidney.

The present study was undertaken to determine organ and tissue radioactivity at post-mortem examination following parenteral administration of Co^{60} vitamin B_{12} to patients with a variety of advanced medical disorders.

Materials and Methods:

Co^{60} vitamin B_{12} having a specific activity of 1.0 $\mu\text{c}/\mu\text{g}$ was used throughout this investigation. The 18 patients selected were under our personal care

and were for the most part in the late stages of malignant diseases, mostly of hematologic origin. Doses of radiovitamin were usually 3.0 μg , administered intramuscularly at South Nassau Communities Hospital and intravenously at Brookhaven National Laboratory. They ranged from 2.0 to 6.0 μg . In patients receiving labeled B_{12} intravenously plasma disappearance and urine and stool excretion analyses were made whenever possible. Some of these data were previously reported. (5) Patients ate regular diets during the entire period and vitamins were neither denied nor prescribed. Death occurred 11 hours to 695 days after $\text{Co}^{60} \text{B}_{12}$ administration. At post-mortem, 2.0 gm of tissue were removed, placed in 4.0 ml vials, digested by the addition of strong acid or base, the contents thoroughly mixed, and radioactivity measured in a well-type scintillation counter. Vitamin B_{12} was calculated as μg per gram of tissue, the entire organ, and a per cent of administered dose. Weight of total body tissues other than those organs measured at autopsy were determined by using per cent of body weight given in tables for standard man. (13) Excretion and tissue distribution were added for total recovery.

Results:

In table 1 are listed patients, diagnosis, interval between injections of Co^{60} vitamin B_{12} and time of death, and organs and tissues containing the highest amount of radioactivity, recorded as per cent of administered dose. As many as 25 organs and tissues were examined from each subject. Because of the unwieldiness of a complete table, only limited and most pertinent data are presented. The liver uniformly contained the highest amount of radioactivity, and varied from 16.6 to 108% of the administered dose. (The latter extraordinarily high levels seen in some cases will be discussed later.) Spleen,

in general, had the next highest levels of activity, ranging up to 13.3%. Next was the gastrointestinal tract, with values up to 9.7%. Following this were kidney with 6.2%, pancreas with maximal content of 4.8%, adrenal gland up to 5.9%, and bone marrow 11.4%. Total recovery, which in some cases included radioactivity in urine and stool, ranged from 45.5 to 168%.

Co^{60} vitamin B_{12} content per gram of wet tissue of each of the patients is shown in figures 1 and 2. In all instances values were adjusted to a standard administered dose of 3.0 μg of the labeled vitamin. Radioactivity in liver corresponding to $\text{Co}^{60} \text{B}_{12}$ ranged from 0.29 μg 5 and 350 days after administration, to 2.75 μg after a 10 day interval. (Fig. 1a) In the spleen low values of 0.01 μg at intervals of 247 and 695 days, up to 1.3 μg 6 days following administration were recorded. (Fig. 1b) The range of values for kidney were not as time dependent as spleen. (Fig. 1c) Low values of 0.03 and 0.045 μg also occurred soon after administration; viz., 5 and 19 days, respectively. A peak value of 0.65 μg was noted on the 10th day. The pancreas did not appear to have any time relationship either. (Fig. 1d) Low values of 0.02 μg were found at 19 and 350 days, while high levels of 0.66 and 0.35 μg were observed after 10 and 52 days, respectively. In the group of adrenal glands, with the exception of one case, all low values were noted after 157 days. (Fig. 2a) These were 0.3 to 14.0 μg . Elevated values occurred on 6, 7 and 10 days post-injection and ranged from 0.66 to 1.33 μg . The opportunity to examine pituitary glands was limited but low and high values were obtained early and late. (Fig. 2b) Bone marrow measurements, never high, ranged from 0.01 to 0.04 μg , the lowest values falling after 74 days. (Fig. 2c)

The distribution of Co^{60} vitamin B_{12} in $\mu\text{g}/\text{gm}$ of wet tissue in individual patients was as follows:

Patient with polycythemia vera who expired 11 hours after administration of radioactive vitamin B₁₂. Liver and adrenal glands contained about 0.5 µµgm per gram of wet tissue. All other organs were 0.25 µµgm or less. (Fig. 3a)

Patient with Hodgkins' disease who expired 3 days after injection of Co⁶⁰ B₁₂ showed the highest concentration in spleen (0.9 µµgm per gram of wet tissue) with pituitary gland, liver, adrenal gland and kidney following in that order. (Fig. 3b)

Patient with carcinoma of the breast, after a similar interval, showed highest concentration in liver, almost 1.0 µµg per gram of wet tissue, with lower values in kidney, spleen and adrenal gland. (Fig. 3c)

Patient with carcinoma of kidney, after a 5-day interval, showed 0.35 µµg per gram of wet liver, with negligible amounts in other organs listed. (Fig. 3d)

Patient with acute myeloblastic leukemia, after a 6-day interval, showed values in liver, spleen and adrenal gland of 1.5, 1.0 and 0.75 µµg per gram of wet tissue, respectively.. It was in this patient from whom we recovered 168% of the administered dose. There were relatively high values, around 0.4 µµgm, in kidney, pancreas and pituitary. (Fig. 3e)

In another patient with acute myeloblastic leukemia and after a 7-day interval, recovery was entirely different. Here adrenal gland had the highest content, 0.65 µµg, liver 0.6 µµg, and other organs relatively little. (Fig. 3f)

In a child with acute lymphoblastic leukemia extremely high levels were found in liver and adrenal gland, with lesser but still elevated values in pancreas, spleen and kidney. Liver contained 2.76 µµg and adrenal gland 1.3 µµg per gram of wet tissue. (Fig. 4a)

A completely different picture was seen in a patient with chronic lymphocytic leukemia, who after a 17-day interval retained minimal values in liver and adrenal gland, and these fell well below the 0.5 μg mark. (Fig. 4b)

Patient with chronic myelocytic leukemia after 19 days, showed 0.85 μg per gram of wet tissue in liver with less than 0.2 μg in kidney, and little else in other organs. (Fig. 4c)

In a patient with carcinoma of lung after a 52-day interval, the liver contained 0.6 μg per gram of wet tissue, with pancreas, adrenal and kidney in the 0.35 to 0.45 μg range. (Fig. 4d)

In chronic lymphocytic leukemia, after 74 days, the $\text{Co}^{60}\text{B}_{12}$ content of liver was 1.25 μg per gram of wet tissue, with bone marrow, kidney and spleen following in order of content from 0.45 to 0.38 μg . (Fig. 4e)

A patient with a brain tumor, after 157 days, had 0.9 μg $\text{Co}^{60}\text{B}_{12}$ in liver, with less than 0.2 μg in kidney, pancreas and adrenal gland. (Fig. 4f)

In a case of chronic lymphocytic leukemia, after 182 days, there were 1.2 μg of $\text{Co}^{60}\text{B}_{12}$ per gram of wet tissue in liver, with the extraordinary amount of 1.0 μg in the pituitary. Spleen was also high (0.5 μg) and kidney contained slightly less activity. (Fig. 5a)

A patient with acute myeloblastic leukemia after 247 days showed very low $\text{Co}^{60}\text{B}_{12}$ content in all organs, the highest being liver (0.4 μg) (Fig. 5b).

Similar low values were seen in a patient with myeloid metaplasia after 350 days, with 0.35 μg per gram of wet tissue in liver. (Fig. 5c)

In chronic lymphocytic leukemia, after 505 days, liver content of $\text{Co}^{60}\text{B}_{12}$ was 0.6 μg per gram of wet tissue, next highest in pituitary and lesser amounts in adrenal gland and kidney. (Fig. 5d)

In a patient with carcinoma of breast, after 580 days, all values were low, the highest being liver with 0.40 $\mu\text{g}/\text{gm}$ wet tissue. (Fig. 5e)

In multiple myeloma, after 695 days, the highest $\text{Co}^{60} \text{B}_{12}$ content was found in pituitary gland (0.4 $\mu\text{g}/\text{gm}$ per gram of wet tissue) and following this was liver. The other organs contained negligible amounts. (Fig. 5f)

Discussion:

Because of the wide range of variation and the great number of organs and tissues examined, correlation of data is extremely difficult. Halstead, Carroll and Rubert reported a seven-fold range in vitamin B_{12} content of some organs in 383 control subjects. (9) In our series there was no apparent correlation of differences with age, sex or diseased state. It was occasionally noted that organs containing metastatic malignant tissue showed extremely high counting rates. Increased tissue binding capacity for $\text{Co}^{60} \text{B}_{12}$ has occasionally been noted in some malignant disorders in this laboratory. (11)

The impossibly high recovery of 168% of the administered dose necessitates comment. The only reasonable explanation is that the liver tissue assayed contained tumor tissue with a high content of B_{12} or was pure liver with a normal content and the product of concentration times abnormal liver weight resulted in a spuriously high recovery. However, this observation perhaps warrants further investigation. The spleen in a case of Hodgkins had a high content and the spleen in the chronic lymphocytic leukemia a low content. Perhaps B_{12} content reflects relative rates of cell proliferation in malignant tissue. In addition, low values may be attributed to various forms of treatment and could have resulted in mobilizing the vitamin from normal storage sites. Similarly, invasion of organs by metastasis may result in eliminating the vitamin

from an otherwise normal storage area. In addition, alterations in growth rate, either due to treatment or the nature of the particular tissue, may vary from patient to patient and within the same subject at different stages of disease.

There is no need to calculate the dose of radiation to the organs since this has been done earlier.(5) In addition, Reizenstein (14) has considered this in detail and at the levels concerned in these studies the dose is well below the established maximum permissible doses.

Conclusions:

1. Following intramuscular or intravenous injection of Co^{60} vitamin B_{12} to patients with various medical disorders between 42.6 and 108% of administered doses was recovered from the organs and tissues at post-mortem examination.
2. Of these values, between 16.6 and 108% was in the liver, with lesser amounts in other organs and tissues.
3. Between one and almost two years after injection 42 to 54% could be recovered from the body and of this 16 to 25% was in the liver.
4. These results are in the main similar to those previously noted in animals and man, with variations depending on species, route of administration, diseased states, and interval between administration and death.

Bibliography

1. Adams, J. F.: The measurement of the total assayable vitamin B₁₂ in the body. Vitamin B₁₂ and intrinsic factor. Second European symposium, Hamburg, 1961. F. S. Verlag, Stuttgart, 1962.
2. Barbee, K. W. and Johnson, B. C.: Metabolism of radioactive vitamin B₁₂ by the rat. Proc. Soc. Exp. Biol. and Med. 76: 720, 1951.
3. Cooperman, J. M., Luhby, A. L., Teller, D. N. and Marley, J. F.: Distribution of radioactive and non-radioactive vitamin B₁₂ in the dog. J. Biol. Chem. 235: 191, 1960.
4. Couch, J. R. and Olcese, O.: The vitamin B₁₂ content of chick tissues as influenced by the diet. J. Nutr. 42: 337, 1950.
5. Cronkite, E. P., Henley, E., Driscoll, D. H., Meyer, L. M., Dohan, F. C., Rubini, J. R. and Wolins, W.: Studies on the kinetics of intravenously injected Co⁶⁰ labeled B₁₂ in man. Hematologica Latina 2: 265, 1959.
6. Doscherholmen, A. and Hagen, P. S.: Alteration of hepatic storage of radiolabeled vitamin B₁₂. Proc. Soc. Exp. Biol. and Med. 95: 667, 1957.
7. Doscherholmen, A., Finley, P. R., and Hagen, P. S.: Distribution of radioactivity in man after the oral ingestion of small test doses of radio-labeled cyanocobalamin. J. Lab. and Clin. Med. 56: 547, 1960.
8. Doscherholmen, A. and Hagen, P. S.: Kinetics of ingested radiocyanocobalamin in man. Vitamin B₁₂ and intrinsic factor. Second European Symposium, Hamburg, 1961, F. S. Verlag, Stuttgart, 1962, p.381.
9. Halstead, J. A., Carroll, J. and Rubert, S.: Serum and tissue concentration of vitamin B₁₂ in certain pathologic states. N.E. J. Med. 260:575, 1959.
10. Meyer, L. M., Berlin, N. I., Jiminez-casado, M. and Arkun, S. N.: Vitamin B₁₂ distribution determined by surface body counting following parenteral

administration of Co^{60} vitamin B_{12} . Proc. Soc. Exp. Biol. and Med. 91: 129, 1956.

11. Meyer, L. M.: Unpublished data.

12. Miller, A., Gaull, G., Ross, J.F. and Lemon, H. M.: Tissue distribution of parenteral Co^{60} vitamin B_{12} in mouse, hamster, rat and guinea pig. Proc. Soc. Exp. Biol. and Med. 93: 33, 1956.

13. Radiological Health Handbook, U. S. Department of Health, Education and Welfare, p.193.

14. Reizenstein, P.: Body distribution, turnover rate, and radiation dose after the parenteral administration of radiovitamin B_{12} . Acta Med. Scand. 165: 467, 1959.

15. Rosenblum, C., Chow, B. F., Condon, G. P. and Yamamoto, R. S.: Oral versus parenteral administration of Co^{60} labeled vitamin B_{12} to rats. J. Biol. Chem. 198: 915, 1952.

16. Smith, E. L.: Vitamin B_{12} . Methuen and Co., Ltd. London, 1960, p.20.

17. Swenseid, M. E., Hvolfoell, E., Schick, G. and Halstead, J. A.: The vitamin B_{12} content of human liver tissue and its nutritional significance. Blood 12: 24, 1957.

Table I. Radioactivity in organs and tissues recorded as per cent of administered dose.

Fig. 1. Radioactivity in (a) liver, (b) spleen, (c) kidney and (d) pancreas recorded as $\mu\text{ugm Co}^{60}\text{B}_{12}/\text{gm wet tissue}$.

Fig. II. Radioactivity in (a) adrenal, (b) pituitary and (c) bone marrow recorded as $\mu\text{ugm Co}^{60}\text{B}_{12}/\text{gm wet tissue}$.

Fig. III. Radioactivity in major organs and tissues recorded as $\mu\text{ugm Co}^{60}\text{B}_{12}/\text{gm wet tissue}$ after (a) 11 hours, (b) 3 days, (c) 3 days, (d) 5 days, (e) 6 days, (f) 7 days.

Fig. IV. Radioactivity in major organs and tissues recorded as $\mu\text{ugm Co}^{60}\text{B}_{12}/\text{gm wet tissue}$ after (a) 10 days, (b) 17 days, (c) 19 days, (d) 52 days, (e) 74 days, (f) 157 days.

Fig. V. Radioactivity in major organs and tissues recorded as $\mu\text{ugm Co}^{60}\text{B}_{12}/\text{gm wet tissue}$ after (a) 182 days, (b) 247 days, (c) 350 days, (d) 505 days, (e) 580 days, (f) 695 days.

Diagnosis	Interval (Days)	Liver %	Spleen %	G.I. Tract %	Kidney %	Pancreas %	Adrenal %	Bone Marrow %	Total %
Poly. Vera	11 Hrs.	23.8	10.8	3.7	1.9	0.4	0.4	11.4	73.6
Hodgkins	3	47.0	2.6	6.0	6.2	0.4	5.0	N.S.	61.5
Breast CA	3	21.4	13.3	4.3	1.8	1.8	0.8	2.7	91.8
Renal CA	5	46.0	0.6	2.0	2.7	1.8	0.2	2.3	59.4
A.M.L.	6	108.0	12.9	9.7	4.1	1.8	0.4	11.4	168.0
A.M.L.	7	43.2	5.1	5.4	2.6	0.5	0.4	10.0	96.3
A.L.L.	10	90.9	7.0	9.0	5.5	1.2	0.3	5.6	129.9
C.L.L.	17	38.0	1.0	6.7	1.4	0.3	0.1	11.1	65.3
C.M.L.	19	41.0	N.S.	2.3	1.3	0.0	0.2	3.6	70.6
Lung CA 2° Poly.	52	26.5	N.S.	8.5	2.5	0.8	0.3	3.9	64.7
C.L.L.	74	27.9	1.9	0.6	1.2	0.3	N.S.	8.4	50.1
Brain Tumor	157	50.0	0.3	1.6	2.0	0.3	1.3	0.7	68.1
C.L.L.	182	65.8	1.5	2.1	0.1	0.1	0.0	1.9	74.7
C.M.L.	234	82.3	13.0	N.S.	3.8	4.8	0.3	N.S.	130.6
A.M.L.	247	31.1	0.0	0.0	1.5	0.4	0.1	0.0	59.8
Myel. Meta.	350	24.9	0.1	1.3	1.0	0.1	0.0	1.2	42.6
C.L.L.	505	20.0	1.9	2.7	1.2	0.1	0.0	5.4	52.6
P.U. Breast CA	580	20.4	0.1	0.5	0.0	0.1	0.0	0.0	53.7
Mult. Myel.	695	16.6	0.5	1.6	1.0	N.S.	0.5	0.5	45.5

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Figure II. Radioactivity in (a) adrenal, (b) pituitary and (c) bone marrow recorded as $\mu\mu\text{gm Co}^{60} \text{B}_{12}/\text{gm wet tissue}$.

Figure III. Radioactivity in major organs and tissues recorded as $\mu\mu\text{gm Co}^{60}\text{B}_{12}/\text{gm wet tissue}$ after (a) 11 hours, (b) 3 days, (c) 3 days, (d) 5 days, (e) 6 days, (f) 7 days.

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