

receiving 120-240 mg of the same died almost immediately, following intracardial injection, from shock symptoms not unlike those described by Kazal *et al.*

Thus it seems clear that, as in the case of alkali-treated bovine serum, alkali treatment of equine serum rendered it practically non-

antigenic, but definitely toxic for guinea pigs. At the same time, it remained practically innocuous for rabbits and for white mice. The toxicity of treated serum for larger laboratory animals and the nature of this toxic substance will be the subjects of further investigation.

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Treatment of Euthyroid Cardiac Patients by Producing Myxedema with Radioactive Iodine.*

HERRMAN L. BLUMGART, A. STONE FREEDBERG, AND ROBERT BUKA.†

From the Department of Medicine, Harvard Medical School, and the Medical Service and Research Laboratories, Beth Israel Hospital, Boston.

Significant clinical improvement in euthyroid cardiac patients following total thyroidectomy has been reported.¹ The rationale of this procedure was verified in that the degree of alleviation of angina pectoris and congestive failure was generally proportional to the degree of reduction in the metabolic rate.² The advent of radioactive iodine has raised the possibility of achieving the same result.

Abstract of Cases. *Case 1.* EM, 46-year-old woman, entered the hospital in 1941 because of progressive ankle edema, dyspnea and orthopnea during the previous year. She had chorea at the age of ten. Physical examination revealed rheumatic heart disease, cardiac enlargement, mitral and aortic stenosis and insufficiency, auricular fibrillation, congestion of the lungs and liver, ankle edema

and orthopnea. She improved after one week in the hospital. In 1942, symptoms and signs of thyrotoxicosis appeared; the basal metabolic rate was approximately plus 33%. A maximal subtotal thyroidectomy was done in 1943. Myxedema developed following this procedure; the signs and symptoms of congestive heart failure markedly improved and she returned to work. Thyroid extract, 0.065 g, was administered daily until January, 1947, when, for the fifth time, the patient entered the hospital with orthopnea, pleural effusion, ascites, and peripheral edema. Thyroid medication was omitted. Despite adequate digitalization, mercurial diuretics, and salt and water restriction, little improvement resulted during 3 weeks of treatment. Following discharge from the hospital, the above signs and symptoms became progressively worse, paroxysmal nocturnal dyspnea appeared, and she again entered the hospital on June 14, 1947. Slight improvement resulted from the above regime of treatment. The basal metabolic rate averaged approximately plus 5%, the serum cholesterol was 220 mg/100 cc. On July, 5, '47, 5 millicuries I^{131} were administered. The total 3-day urinary excretion was 71%. Approximately 10 weeks later the basal metabolic rate was minus 14% and the serum cholesterol 400 mg %. On November 1, '47, 13.6 millicuries I^{131} were administered. A tracer study on December 4, 1947, showed

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¹ Blumgart, H. L., Levine, S. A., and Berlin, D. D., *Arch. Int. Med.*, 1933, **51**, 866.

² a. Blumgart, H. L., Berlin, D. D., Davis, D., Riseman, J. E. F., and Weinstein, A. A., *J. A. M. A.*, 1935, **104**, 17; b. Blumgart, H. L., Riseman, J. E. F., Davis, D., and Weinstein, A. A., *Am. Heart J.*, 1935, **10**, 596.

84% excretion in 3 days. On December 10, '47, 6 weeks after the second dose, the basal metabolic rate was minus 26% and the serum cholesterol 440 mg %. Clinical evidence of myxedema, including lethargy, hoarseness, dry hacking cough, cold dry yellow skin were present. Her cardiac status improved. She was able to sleep flat in bed and undertake considerably more effort without dyspnea. Peripheral edema reaccumulate more slowly and, therefore, mercurial diuretics were required less frequently. Thyroid extract, 6 mg per day, mitigated the symptoms of myxedema and has enabled the patient to maintain clinical improvement.

Case 2. 60-year-old man entered the hospital for the fifth time on June, 1947, because of progressive cyanosis, dyspnea, orthopnea, hydrothorax, and nightly attacks of acute paroxysmal dyspnea. He had been treated in the out-patient department and wards for more than 5 years. The clinical diagnoses were arterial hypertension, rheumatic heart disease, mitral and aortic stenosis and insufficiency, marked cardiac enlargement, auricular fibrillation, arteriosclerosis of the coronary and peripheral arteries, and congestive heart failure. Despite treatment including optimal digitalization, mercurial diuretics, restricted fluid and salt intake, and curtailment of activity, his clinical status became progressively worse. Following admission to the hospital, treatment, including the removal of 1700 cc from the right chest which had accumulated in one week since previous thoracentesis, resulted in slight improvement, but he continued to have paroxysmal dyspnea and was considered critically ill. Basal metabolic rates ranged from plus 8 to minus 8% and the serum cholesterol level was 200 mg %. Ten millicuries I¹³¹ were administered on July 5, 1947. The total 3-day urinary excretion was 51%. On September 18, 1947, an additional 2.25 millicuries of I¹³¹ were administered. Four weeks later, or 3½ months following the first dose, the basal metabolic rate had declined to minus 25% and the serum cholesterol increased to

600 mg %. Coincidentally, the clinical status of this patient improved. He was able to sleep uninterruptedly flat in bed and dyspnea was much less, despite increased activity up and about on the ward. Reaccumulation of fluid has been slower and he requires fewer injections of mercurial diuretics.

Discussion. In both patients, the uptakes of tracer doses of I¹³¹ were consistent with results obtained in subjects with normal thyroid glands. The normal basal metabolic rates, the normal serum cholesterol values, the normal cardiac rates and the absence of any clinical evidences of thyrotoxicosis were consistent with the normal thyroid state. The elevation of the serum cholesterol values in reciprocal relation to the fall in the basal metabolic rates which occurred gradually as the clinical evidences of myxedema appeared, demonstrate that radioactive iodine produced hypothyroidism in these two patients. The clinical improvement concomitant with reduction in metabolic rate observed in these two patients was similar to that observed in previous studies of cardiac patients following surgical total thyroidectomy.²

Considerable attention was given to possibly toxic effects of the rather large doses of radioiodine administered to these patients. Our studies have failed to disclose such evidence. The optimum dosage and regime of administration of I¹³¹, the regularity with which myxedema may be induced in such patients, the possible utilization of adjuncts, such as thiourea derivatives and thyroid stimulating hormone of the pituitary, and final appraisal of the clinical value of this procedure, are matters under investigation which prolonged and extensive studies and observations will clarify.

Summary. Radioactive iodine 131 was administered to 2 severely ill cardiac patients who showed no clinical or laboratory evidences of thyrotoxicosis or myxedema. In both instances, decided reduction in the metabolic rate coincided with clinical improvement. These results justify further studies and observations.