VISUALIZATION OF THE GALLBLADDER BY THE SODIUM SALT OF TETRA-BROMPHENOLPHTHALEIN *

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Since the publication of an article a few weeks ago by two of us [1] on the production of roentgen-ray shadows of the gallbladder, a more satisfactory method has been developed by using the sodium salt of tetrabromphenolphthalein, instead of the calcium salt. The sodium salt is much more soluble. We are now using only from 35 to 40 c.c. of solution instead of 350 c.c. required by the calcium salt. It is much more stable, and is not crystallized out by sterilization. The first several injections of the calcium salt, as stated in our previous publication, produced no reaction. However, it was found later that a large proportion of the patients had reactions, which were characterized by headache, backache, nausea and vomiting, which lasted from ten minutes to ten hours. There were never any significant changes in pulse or blood pressure. The sodium salt was found to produce much less severe reactions; in fact, a large percentage of the patients had no ill effect, except a transient nausea lasting only ten or fifteen minutes. Particularly was this true among the men patients, who as a whole seem less susceptible to reaction. It seems quite probable that the large amount of fluid used in the injection of the calcium solution was responsible for part of the reaction.

The sodium salt of tetrabromphenolphthalein can now be obtained in crystalline form from the Mallinckrodt Chemical Works of St. Louis. If this is used, all that is necessary to do is to dissolve 5 or 5.5 gm. of the crystalline salt by heating in 40 c.c. of distilled water, and sterilize in a boiling water bath for fifteen or twenty minutes. A few samples have been autoclaved, and were found to produce shadows just as efficiently as the solution sterilized in the water bath. If desirable, the solution may be put up in vials, sealed and sterilized. These solutions, as well as those in unsealed receptacles, have been left for from twenty-four to thirty-six hours before injection and found to be just as satisfactory as those given immediately after preparation. As yet we have not given a solution that has been standing over thirty-six hours, but see no reason why it should acquire any harmful properties.

The solution of the sodium salt is given intravenously, preferably in two doses. We have never given it all in one dose, and do not know whether any serious symptoms would result or not. The injection should be given in the morning between 7:30 and 9:30 with a syringe, in divided doses as stated, after the solution is warmed to body temperature. The dose should be reduced for patients weighing less than 115 pounds (52 kg.). Great care should be taken not to allow extravasation of the solution outside the vein, on account of the danger of necrosis. To obviate this danger, we recommend dilution of the solution up to 40 c.c. and insertion of the needle independently of the syringe, thus allowing a free flow of blood before the solution is injected. A few cubic centimeters of sterile physiologic sodium chlorid solution should be injected after the dye to prevent leakage of the solution through the vein wall or needle.

Orders are given for the patient to:

1. Omit breakfast.
2. Omit lunch (a glass of milk may be given if hunger is too pressing).
3. Take 40 grains (2.6 gm.) of sodium bicarbonate every three hours for forty-eight hours day and night while awake.
4. Lie on the right side of the abdomen or be up.
5. Take water, if desired, by mouth.
6. Omit protein from the evening meal on the day of injection.
7. Take roentgen-ray films at four, eight, twenty-four and thirty-two hour periods (no special technic).

We call attention especially to the omission of breakfast and lunch, since this was unfortunately not mentioned in our first publication, and seems to be of great importance.

ANALYSIS OF CASES

There have been fifty-five cases in which injections with adequate dosage were given. One of these had inadequate roentgen-ray films. Several experimental routines were tried. The one given above seems to produce, by far, the most satisfactory results.

Results

Regular routine	Calcium salt...	28	25 positive	
			3 negative.....	2 had obstruction of cystic duct with stones
				1 had gallbladder only 2×3 cm. in diameter and very badly diseased
	Strontium salt	2	faintly positive	
	Sodium salt...	10	9 positive	
			1 negative (appendiceal abscess; gallbladder not seen)	
Experimental routine	1. Combined with gastro-intestinal roentgen-ray series.....	9	7 positive	
			2 negative	
	2. Variation of routine orders.....	3	negative	

INTERPRETATION OF RESULTS

Obviously, any attempt to establish a criterion for the diagnosis of lesions of the gallbladder from the roentgen-ray shadow at such an early date would be entirely premature. However, certain features have presented themselves, many of which have been quite consistent.

A normal gallbladder will begin to cast a shadow from three and one-half to five hours after the injection; will show a tendency to change in size; will cast its heaviest shadow between sixteen and twenty-four hours, and empty in about forty-eight hours. The shadow shown on the four or eight hour plate is almost invariably larger than the subsequent shadows. So far, all gallbladders that failed to show this "elasticity or distensibility" at some time during the series, when the injection was followed by the routine given above, have been found to be pathologic at operation, or to give definite clinical findings of gallbladder disease. Pathologic gallbladders do not cast so heavy a shadow as normal ones, since the production of the shadow is dependent on the concentration power, which may be partially or completely destroyed by disease. In four cases in which the routine order was followed, the gallbladder failed to cast a shadow. All of these patients were operated on. Two had a stone occluding the cystic duct; one had a gallbladder so scarred and contracted by disease that it was too small to cast a shadow. The fourth patient had an appendical abscess containing a considerable amount of pus; on account of the abscess,

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1. Graham, E. A., and Cole, W. H.: Roentgenologic Examination of the Gallbladder, J. A. M. A. 82:613 (Feb. 23) 1924.

the gallbladder region was not explored, and the amount of pathologic change, if any, could not be determined.

In all patients with cholelithiasis in which the cystic duct was not occluded, the stones have appeared as either negative or positive shadows, but only after the injection of the dye. The size, shape and density of the roentgen-ray shadows of the gallbladder have been variable, and will undoubtedly prove to be important factors in diagnosis. It is most important, as in gastrointestinal examination by roentgen ray, that a series of plates be obtained. So far, we have been content with four, eight, twenty-four and thirty-two hour plates.

SOME CHANGES IN THE CHEMICAL CONSTITUENTS OF THE BLOOD FOLLOWING A MARATHON RACE

WITH SPECIAL REFERENCE TO THE DEVELOPMENT OF HYPOGLYCEMIA *

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Last year we [1] studied a group of runners who participated in the American marathon race of 25 miles, which takes place annually in Boston, April 19. In general, it was found that men who had been doing long distance running for many years did not develop hypertrophy of the heart as indicated by roentgen-ray examination. Furthermore, directly after the race, the heart was found to be somewhat contracted rather than dilated. The vital capacity of the lungs was measured and did not seem to bear any particular relation to the running ability of the contestants, and on the average it was not increased over the normal figure for men who live comparatively nonathletic lives.

This year the usual distance of 25 miles was extended to 26 miles and 385 yards, the occasion being the final Olympic tryout. The examinations this year were made to see what changes occurred in some of the more important constituents of the blood, i. e., the sugar, uric acid, nonprotein nitrogen and carbon dioxid combining power. In all, eleven different runners were examined. Of these, five (Runners 57, 59, 55, 1 and 46) were tested one or two days before the race. One of the others (Runner 68) was not only examined directly after the race but returned two days later for final observation. Since many of the contestants had come from a considerable distance, and had arrived in Boston only the night before the race, it was not possible to examine the other five until immediately after the race. The plan was to draw venous blood from the arm as soon after finishing the race as possible. In the five men who had control specimens taken before the race, this was done within ten minutes after they had crossed the finish line. In a few, blood was taken within two minutes. With the others venipuncture was made somewhat later, but in no instance did more than thirty minutes elapse between the finish and the bleeding. The blood was drawn into lithium oxalate, and determinations were made within one to two hours by the methods of Folin according to his latest modifications.

BLOOD CONSTITUENTS AFTER RACE

In the table are charted the data obtained in this study. Several striking points are apparent. The nonprotein nitrogen practically doubled in all instances. This bears out the work done by Feigl,[2] who found a somewhat similar rise in the blood constituents of German soldiers following a 20 mile march with full packs. The uric acid showed a decided increase above the normal. Although only one runner was reexamined (Runner 68), the examination showed that the nonprotein nitrogen and the uric acid had returned to normal forty-eight hours after the race. The carbon dioxid combining power of the blood showed a slight but distinct tendency to fall in three runners on whom control determinations were made before the race.

The most striking feature of the study was the marked fall in the sugar content of the blood that occurred in a majority of the runners. An analysis of the individual findings proves rather illuminating. No. 60 showed a rather high blood sugar level, 178 milligrams per hundred cubic centimeters. This runner left the race at about the fifteenth mile, and took some food, consisting of meat, bread and soda water, from fifteen to thirty minutes before the blood was drawn. Runner 68 also showed a slightly elevated blood sugar level; this was accounted for by the fact that he ate some food just as he finished the race, and about twenty minutes before the blood was taken. There were three men (1, 46 and 79) whose blood sugar was within normal limits. The first two of these had had preliminary examinations, and the figures after the race, which are lower, show that the fall may have resulted from the violent exercise, although the element of variation of blood sugar content with relation to the previous meal was a possible factor in the change. The remaining six runners showed unusually low blood sugar levels after the race.

Observations After Race

Number of Runner	Mg. per 100 C.c. of Blood Plasma: Nonprotein Nitrogen Before	Nonprotein Nitrogen After	Uric Acid Before	Uric Acid After	Sugar Before	Sugar After	Carbon Dioxid Combining Power Before	Carbon Dioxid Combining Power After	Physical Condition
57	28.20	54.00	2.88	5.16	81	65	37.3	33.5	Fair (pale)
59	29.40	58.80	5.72	6.33	87	49	41.8	37.3	Very poor (pale, cold) irritable
55	23.40	36.90	4.44	7.00	88	65	43.2	34.0	Fair
1	26.70	34.50	3.0	3.40	108	89	....	....	Good
46	25.20	36.90	3.68	6.20	92	82	....	41.8	Good
68	.....	38.10	....	6.88	..	123	....	....	Good; ate food before venesection
		23.50*		3.80*		91*			
60	.....	39.30	....	4.92	..	178	....	....	Good; stopped running after 15 miles; ate food before venesection
79	.....	63.60	....	7.13	..	82	....	....	Good
109	.....	30.30	....	4.24	..	50	....	....	Very poor (pale)
29	.....	45.00	....	6.58	..	47	....	34.0	Very poor (pale)
37	.....	32.40	....	5.56	..	45	....	....	Very poor, shocked, stuporous

* Blood taken forty-eight hours after the race.

Such figures are rarely encountered in human experience except with excessive doses of insulin. In some experimental work by Mann and Magath [3] on dogs, the sugar content of the blood was found to fall to low levels following the complete extirpation of the liver. They found that at the level of 60 mg. per hundred cubic centimeters, the animals became weak. On reaching 50 mg., the muscles became flaccid and the animals

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2. Feigl, J.: Chemische Blutuntersuchungen an der Teilnehmern eines Armes, Gepäckmarsches, Biochem. Ztschr. **86**: 292, 1916.

3. Mann, F. C., and Magath, T. B.: The Liver as a Regulator of the Glucose Concentration of the Blood, Am. J. Physiol. **55**: 285, 1921.