groups of rabbits over a period of one year after the injections. The altered serum cholesterol appeared more rapidly in those animals receiving DNA and citrate. The changes observed in the group injected with 0.1 mg DNA and 30 μMoles citrate were comparable to those of the group injected with 30 times as much DNA without citrate. Previous quantitative studies(3) had shown that over this same dosage range the time required for the appearance of the serum cholesterol changes varied inversely with the amount of DNA injected. Therefore, it appeared that *in vivo* inhibition of the plasma deoxyribonuclease by sodium citrate in this experiment had increased 30-fold the effectiveness of the injected DNA.

Discussion. The data presented indicate that injection of sodium citrate produces a significant *in vivo* inhibition of the deoxyribonuclease circulating in blood. The effectiveness of the injected DNA in lowering serum cholesterol levels was markedly increased when it was injected together with citrate. Injection of 0.1 mg DNA with a measurable, transient, enzyme inhibition lasting 30 minutes resulted in quantitative effects comparable to 3 mg DNA injected without citrate. This 30-fold greater effect suggests that the DNA injected without citrate in this, and in previous studies(1,3), has been largely inactivated (at least 97%) in the bloodstream prior to absorption into cells. It also serves to emphasize the exceedingly small quantities of "active" DNA needed to induce the prolonged alterations of serum cholesterol regulation.

It is noteworthy that a 2-fold inhibition of the plasma deoxyribonuclease as determined by viscosity measurements was associated with a 30-fold increase in physiologic activity of the DNA. A similar disproportion between viscosity changes and biologic activity was observed by Zamenhof and his colleagues (7) in the effect of crystalline deoxyribonuclease on bacterial transforming DNA. Incubation of small amounts of the enzyme with the DNA resulted in loss of 100% of the biologic activity and only a 10% decrease in the viscosity.

Summary. Sodium citrate injected into rabbits in amounts ranging from 9 μMoles to 150 μMoles produces a transient, significant *in vivo* inhibition of the plasma deoxyribonuclease. Injection of heterologous DNA into rabbits induces a prolonged decrease in total serum cholesterol. 30 μMoles of citrate and 0.1 mg DNA, injected together, are quantitatively as effective as 3 mg DNA in altering the serum cholesterol regulation. The citrate-induced deoxyribonuclease inhibition increased the physiologic activity of the injected DNA as much as 30-fold.

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Received June 12, 1961. P.S.E.B.M., 1961, v107.

In vivo P^{32} Radioautography in Detecting Breast Cancer.* (26774)

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A method of *in vivo* radioautography of the stomach based on selective uptake of P^{32} by malignant tissue, and employing a balloon coated with a photosensitive emulsion, has been described(1,2). Adaptations of this method for various other organs are being explored. The purpose of this communication is to report upon our experience with

* This work was supported by a grant from Am. Cancer Soc. and Atomic Energy Commission.

the method in the recognition of breast cancer.

Method. Patients for this study have come from the in-patient services of the University of Minnesota Hospitals. They include a group of women and one man. In most instances, these patients had been admitted for investigation of breast masses. Usually, a normal contralateral breast has been studied as a control. Occasionally, our examination has concerned a patient in whom the diagnosis already was known on the basis of prior excisional biopsy. In such patients, frequently no tumor is detectable in the breast upon its removal, even on histologic examination. Two such patients are included in this study. In a few patients under scrutiny for evidences of a gastric lesion, breasts were screened simultaneously while P^{32} studies were underway.

The patient is admitted to the hospital in the afternoon and receives a large tracer dose of sodium radiophosphate (500 μc) intravenously. A shield composed of a photosensitive emulsion coated on a vinyl plastic backing is then immediately applied to the breast while the patient is in the dark room. A heavy dressing of compresses and elastic Ace bandages is then applied so that all possible sources for light leaks are blocked out. Flattening of the breasts to distribute tissue mass is accomplished by this dressing. The bandage is left in place overnight for 18 hours and removed in the morning. The appearance of a dark area on the breast mold after developing the emulsion by immersion in developer and fixing solutions suggests the presence of a malignancy, owing to the greater affinity of neoplastic tissue for P^{32} over the adjacent normal tissue.

It has been necessary to secure adequate separation of emulsion from the skin to preclude destruction of the former by perspiration or its adherence to the skin. For this reason, a thin layer of Saran-wrap is applied directly to the skin and the shield is applied over it. Lubrication of the Saran-wrap itself, with powder or with glycerine, insures that the emulsion will separate readily when the test is concluded.

Modifications in technic have all been related to determining a suitable substance for a shield backing. Rigid molds of vinyl plastic coated with emulsion and molds of softer plastic with emulsion coatings have been employed as well as coated sheets of latex rubber, and emulsion-coated balloons. Currently, balloons and molds of soft flexible plastic are under investigation. The emulsion can be kept within a balloon and thus be protected from the skin. A certain degree of conformity to the breast can be achieved by pressure on the balloon alone. The use of a flexible soft plastic backing is much more comfortable for the patient and easy to handle for the operator. This can be molded to the breast readily. The problem of protection of the emulsion from the skin with this preparation does still exist, however.

TABLE I.

No. of patients	Diagnosis	Operation	Autograph
4	Cancer	Rad. mast.	+
8	Benign disease	Biopsy	7 − 1 +*
5	" "	0	—
10	Normal	0	—
2	Cancer totally excised by prior biopsy	Rad. mast.	1 − 1 +†
2	Old mastectomy scar no recurrence	0	—

* 1 false positive-light leak.
† 1 false positive-fresh biopsy site.

All of the above preparations have been coated by the Eastman Kodak Co., Rochester, N. Y., who have also supplied the plastic backings. Latex sheets and balloons have been supplied by National Hygienic Products Co., Akron, Ohio.

Results. To date, 31 breasts have been studied successfully (Table I). Four cancers not previously operated upon all gave a positive response. Ten normal breasts gave negative results. Seven of eight breasts with benign disease confirmed by surgical removal and histologic examination likewise were negative. Five breasts believed on clinical grounds to be benign were negative on radioautographic study and have yet not been operated upon.

In 2 additional instances, old mastectomy wounds, without any physical evidence of re-

currence, were studied. Both of these studies were negative. In another instance, a false positive response was associated with a benign lesion and is felt to represent an artifactual light leak. In one other instance a positive study was obtained in a breast with a fresh biopsy wound. No residual tumor histologically was present in the breast. In the final instance, a negative study was obtained in a patient who had had an excisional biopsy some time before the study. No residual tumor was present in this breast either.

Discussion. P^{32} has been employed by Nakayama in detection of esophageal and gastric neoplasms by using a Geiger-Mueller tube for detection(3). Neoplasms of cervix and vagina have likewise been studied by Geiger-Mueller tube counting(4,5). There have been numerous studies on the use of this method to diagnose cancers of the breast (6-9). Accuracy has been reported as high as 85% to 90% in several studies, but the method is tedious and permits identification of only fairly large and superficial lesions. Radioautographic methods seem to be more successful because they allow a long exposure of the recording medium to the surface being studied. This permits identification of areas with only slightly increased radioisotope content. Statistical errors associated with short-term counting technics are also avoided. Therefore, we felt that a recording exposure of some length would allow us to detect lesions in the breast with more accuracy than that obtained with a counter. In addition, the entire breast is scanned for areas of increased P^{32} content.

This test, it must be emphasized, is as yet developmental. We are presenting our initial experiences with it, which are encouraging. The penetration of P^{32} beta particles in tissue is no longer than 0.7 cm; however, the breast, compressed with a dressing to a minimal thickness and studied over a period of 18 hours apparently concentrates enough beta particle activity and secondary radiation to permit small increases of P^{32} activity to be detected by a sensitive emulsion.

This technic will be expanded and, together with technics for screening of the stomach, cervix and colon which are being developed at this hospital may afford an opportunity for screening of many areas of the body with one dose of P^{32}.

Summary. A method of *in vivo* radioautography of the breast as a screening procedure for breast neoplasms, using P^{32} has been presented and discussed. Thirty-one cases with 2 false positive results and no false negative results have been presented.

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Received June 12, 1961. P.S.E.B.M., 1961, v107.