TECHNICAL PAPERS

Suppression of Gastric Acidity with Beta Particles of P^{32}

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Irradiation of the gastric mucosa by X-rays or gamma rays of radium has suppressed gastric acidity (*2, 3*). Such irradiation penetrates and affects not only the gastric mucosa, but also adjacent organs. The liver and small intestine are more sensitive than the gastric mucosa to radiation (*1*), and damage to these adjacent organs may occur if large doses of X-rays or gamma rays are directed to the stomach.

To suppress acidity, it would therefore seem more suitable to restrict radiation to the gastric mucosa. This is accomplished by the topical application to the mucosa of a radiation source emitting rays which are absorbed almost completely by the stomach. A suitable source is the radioactive isotope of phosphorus, atomic weight 32, for this isotope emits beta particles whose maximum range in tissue is about 8 mm. An applicator was devised to apply P^{32} topically to the mucosal lining of Heidenhain stomach pouches in dogs.

The applicator was a thin rubber bag inflated to a volume of 50 cc with air, sprayed with rubber cement, and covered with flocs of short cotton fibers, so that the covering resembled a smooth coat of felt. The inflated balloon was dipped into a solution containing P^{32} and allowed to dry. By a series of these dippings and dryings as much as 25 mc of P^{32} was adsorbed uniformly on the flocculate surface of the balloon. The balloon was then deflated, covered by a rubber condom, inserted into the Heidenhain pouch, and reinflated with air to its original volume of 50 cc. The condom covering the balloon prevented loss of P^{32} from the felt-like surface and only adsorbed 4% of the beta activity.

A series of control observations were made on the secretion of Heidenhain pouches with histamine as a stimulus. Then the pouches were irradiated.

After exposure to this beta radiation for periods of 2–6 hr the balloon was deflated and withdrawn. Subsequently, acid secretion tests were again made with the same stimulus of histamine used in control secretion observations. The pouch mucosa was observed by cystoscope, and multiple punch biopsies of the mucosa were made in some of the animals at frequent intervals.

The maximum thickness of the mucosa of these Heidenhain pouches is about 4 mm, and the average thickness is about 3 mm. At a depth of 3 mm the dose is about 25% of the dose in the first mm of mucosa. The thickness of the whole pouch wall is about 7–8 mm, at which depth the dose has decreased to less than 2% of the dose to the first mm of mucosa. Preliminary histological examination of a post-mortem specimen indicates that there is no discernible change in the serosa of the pouch when the mucosa has been heavily irradiated.

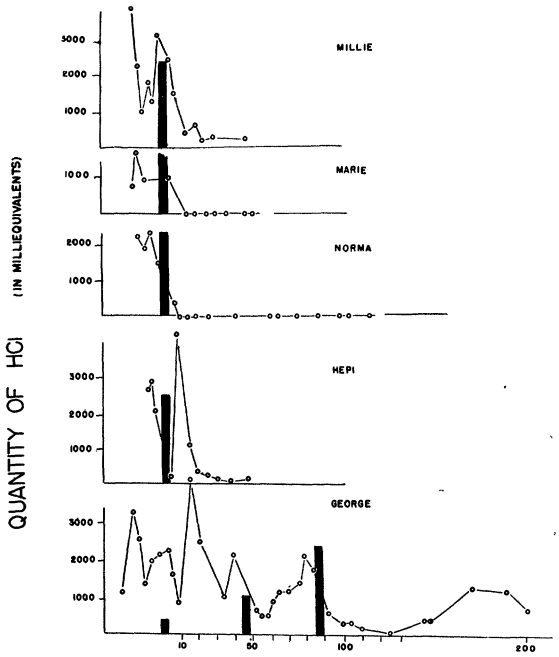

FIG. 1.

Radiation was followed after a few days by a decrease in total secretion as well as a decrease in quantity and concentration of HCl in the pouches of all five dogs studied. Two of these five dogs had anacid pouches, and the other three were hypoacid. Intubation of the stomach during the course of these secretion tests with histamine stimuli showed that the secretion of the true stomach had a pH of 1.0 at the same time the pouch secretion had a pH of 7.0.

Fig. 1 shows the change in pouch acid secretion after radiation. All radiation exposures yielded doses in the magnitude of 20,000 to 25,000 equivalent roentgens to the first mm of tissue except for the preliminary radiation on George (lowest graph in Fig. 1).

The heavy vertical bars in this instance represent respectively 1,800, 12,000 and 25,000 equivalent roentgens in the first mm of mucosa. Although the decrease in acidity with the lower doses was not apparent, the higher doses invariably decreased pouch acidity. All other vertical heavy bars in Fig. 1 represent radiation

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exposure of 20,000 to 25,000 equivalent roentgens to the first mm of tissue. A few weeks after radiation, the quantity of acid secreted had decreased to levels ranging from anacidity to 10% of the quantity secreted before radiation. The longest period of observation after radiation in any animal was 125 days.

There were no changes in blood count, weight, or general condition of the animals which could be attributed to the radiation.

In summary, the gastric mucosa of Heidenhain pouches of five dogs was irradiated with beta particles of P^{32}, with a resultant marked decrease in the quantity of acid in the pouch secretion.

If similar techniques in humans are contemplated it is important to note that the dog Hepi had return of acidity in its Heidenhain pouch 3 months after irradiation. When the animal was sacrificed two weeks later, autopsy showed an ulcer of the pouch mucosa at the site of previous biopsy.

References

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β-Glucuronidase Activity

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During the past few months, a method has evolved which gives promise as a diagnostic aid in female genital carcinoma. Fishman (*1*) first reported an increased activity of the enzyme β-glucuronidase in carcinoma tissue (breast, esophagus, stomach, and colon). Subsequently (*2*), results from other malignant tissues were added to his series. The possibility of measuring the tissue activity of β-glucuronidase from the more accessible pelvic malignancies (vulva, vagina, and cervix) as a diagnostic aid is self-evident. Furthermore, if present indications prove correct, the vaginal fluid which bathes the cervix and vagina should become a rich source of this enzyme in the presence of a lower genital tract malignancy.

Accordingly, β-glucuronidase assays were made on the various genital tissues and on vaginal fluid for the purpose of establishing the range of activity in histologically benign lesions, and in carcinoma. Tissues were weighed, homogenized in water, and the centrifuged homogenates assayed, using phenolphthalein glucuronide as substrate, according to the method described by Fishman, Springer, and Brunetti (*3*). Using a pipette, 0.1-ml portions of vaginal fluid were suspended in 3 ml of distilled water or Tyrode's solution. Assays were made on both uncentrifuged specimens and on the centrifuged supernatants. Values were expressed as γ of phenolphthalein liberated per g of tissue or ml of vaginal fluid per hr. Our results are tabulated.

In the absence of pregnancy, the range of β-glucuronidase activity in those cervices without histological evidence of malignancy was from 23 to 330 γ of phenolphthalein per g tissue per hr (Table 1). The upper limit of this group was significantly less than the lowest value for cervical carcinoma, 543 γ, #299510 (Table 2).

TABLE 1

GLUCURONIDASE ACTIVITY

Tissue	Cases	γ of β-Glucuronidase*	
		Range	Average
Benign cervix	13	23– 330	142
Pregnant cervix	8	221– 591	384
Malignant cervix	6	543–2790	1274

* β-Glucuronidase expressed as γ phenolphthalein liberated per g of tissue per hr.

A variety of clinical and pathologic diagnoses were found among the benign cervices studied. Most were from cervical biopsies obtained to rule out malignancy. Others included senile vaginitis, cervical erosion, acute and chronic cervicitis, and some apparently normal organs. A histologic examination of the tissue adjacent to the area assayed established an absence of malignancy. The activity of b-glucuronidase in vaginal mucosa (nonpregnant) was similarly low. The enzyme activity of pregnant cervix (at term) was higher, and there was some overlapping with the malignant group. No explanation is offered at the present time for this finding.

TABLE 2

GLUCURONIDASE ACTIVITY OF UNTREATED CARCINOMA TISSUE

Identification	Microscopic diagnosis†	γ of β-Glucuronidase‡
436773	Sq. ca. cx.	934
438049	Sq. ca. cx.	2790
159341	Sq. ca. cx.	1634
452839	Sq. ca. cx.	847
299510	Sq. ca. cx.	543
45424	Sq. ca. cx.	897
A.M.*	Sq. ca. vag.	688
A.S.*	Sq. ca. vag.	680

* Patient at another hospital.

† Sq. ca. cx.—Squamous carcinoma of cervix; Sq. ca. vag.—squamous carcinoma of vagina.

‡ β-Glucuronidase expressed as γ phenolphthalein liberated per g of tissue per hr.

The malignant tissues studied are tabulated in Table 2. The range of activity was high. Two specimens of endometrial carcinoma were assayed. These measured 11,930 and 6,370 γ. The lower of these values is within the range of glucuronidase activity for endometrium in women with normal menstrual periods (895 to 9040 γ) (*4*) and both are well within the range for endometrium in patients with functional uterine bleeding (1,180 to 20,050 γ) (*5*). The activity of β-glucuronidase in normal ovary and in benign ovarian tumors varied greatly. It