increases in blood pressure and serum potassium were comparable with those shown in Fig. 1. In consideration of the large dose, however, these increases were slight since greater effects are obtained even with 0.1 mg per kg of epinephrine.[5] Two samples of reaction mixture No. 2 were prepared in which potassium permanganate was added to supply 2½ atoms of oxygen per molecule of epinephrine. Each was tested on a cat. The serum glucose was little affected as with reaction mixture No. 1. The blood pressure however showed a fall instead of a rise in both animals. In one animal the serum potassium rose (Fig. 3) as it did with reaction mixture No. 1 but in the other it showed no change. These experiments although few in number gain significance by the fact that the regularity and degree of blood pressure and serum potassium changes produced by epinephrine have been previously established,[5] the same being true for the serum glucose changes as reported in the first part of this paper. Consequently any deviation from this constant effect is striking. These results suggest an independence of the three effects since in the oxidation of epinephrine they are not modified in parallel. The elimination of the serum glucose effect even before those of blood pressure and serum potassium would not support the postulation made above that this action is due to a decomposition product of epinephrine.

Summary. In a series of experiments on cats the changes in serum glucose, serum potassium and blood pressure produced by epinephrine were compared chronologically. The rise in serum potassium occurs later than the rise in blood pressure while the rise in serum glucose begins still later and is much more prolonged than the other 2 effects. This indicates that epinephrine hyperglycemia is independent of the serum potassium increase. As further evidence it is shown that in the oxidation of epinephrine by potassium permanganate the above actions are not modified in parallel.

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Tumor of Rat Testis Produced by Heterotransplantation of Infantile Testis to Spleen of Adult Castrate.

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In a previous report,[1] we have described the development of granulosa cell tumors of the rat ovary after transplantation of one ovary to the spleen and removal of the other. With this technic, the estrogen produced by the transplanted ovary is secreted into the portal circulation and inactivated in the liver. The estrogen is thus prevented from exerting its normal cyclic inhibiting effect on the pituitary. The excessive secretion of pituitary gonadotrophin which thus results is enabled to act continuously on the transplanted gonad.

The present communication is concerned with application of this technic to the production of neoplasm of the rat testis. Implantation of an entire adult testis into the spleen of the same rat is impossible owing to the comparatively large size of the former organ; only small amounts of testicular tissue can thus be implanted. However, heterotransplantation of the testis of an infantile rat, from 9 to 14 days old, into the adult spleen, is comparatively as simple as similar ovarian

* Aided by grants from the Lederle Laboratories, Inc., the Winthrop Chemical Company, Inc., and the United Hospital Fund of New York.

1 Biskind, M. S., and Biskind, G. R., PROC. SOC. EXP. BIOL. AND MED., 1944, **55**, 176.

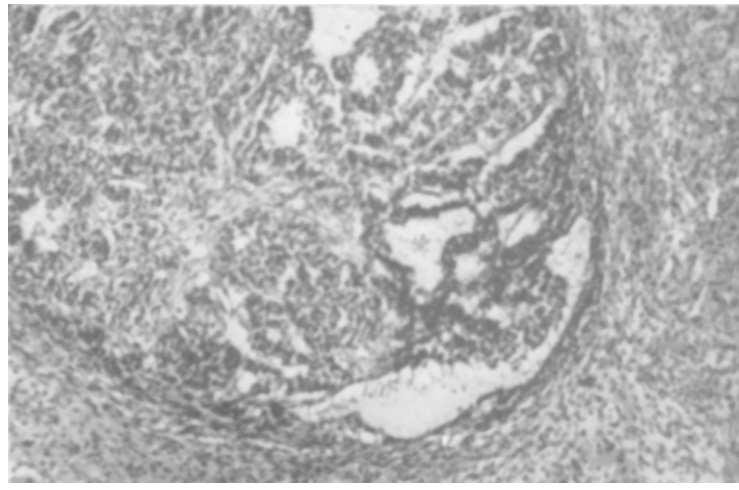

FIG. 1.
Nest of "granulosa" cells in interstitial cell mass. (About 90 ×.)

transplantation.

Accordingly, adult rats of the Sherman strain were castrated and a testis from an infantile rat of the same strain was implanted into the spleen of each. Similar implantation was also made into the spleens of noncastrate animals. The animals were killed at intervals of from 8 to 11 months after the implantation.

In 2 animals that had not been castrated, the implants had increased from an original size of about 5x2x2.5 mm to 8x5x5 mm and 11x5x5 mm in 8 months. In both cases, there was extensive degeneration of the tubules and little remaining interstitial tissue on microscopic examination. There were numerous large cystic areas.

In animals that had been castrated at the time of implantation, the picture was different. In one animal the transplant had increased in size from about 4x1.5x2 mm to 11x9x6 mm in 9 months. In another, the transplant grew in size from 5x2x2.5 mm to form a tumor 21x12x12 mm in size in 11 months; the latter was the largest of all the implants in this series (and exceeded the size of a normal adult rat testis); it formed an irregular, nodular mass which protruded at intervals from the surface of the spleen. In every case, in the animals that had been castrated before the transplantation was made, the prostate and seminal vesicles were atrophic, grossly and histologically, and the hypophysis showed the typical castrate change, indicating that no significant portion of the androgen secreted by the implanted gonad, escaped inactivation in the liver.[2]

Histologically, the large tumor is distinctly demarcated from the splenic substance by a laminated band of fibrous tissue that varies in thickness. Some strands of fibrous tissue arise from this capsule and radiate for variable distances into the tumor. Two distinct cellular components are readily recognized (Fig. 1 and 2), for the most part sharply demarcated from each other but in a few places intermingled. The major component is composed of a solid sheet of relatively large polyhedral cells that are compactly arranged and poorly outlined. They have a granular eosinophilic cytoplasm that may contain an irregular vacuole. The nucleus is round and contains many fine chromatin granules and a small basophilic nucleolus. An occasional mitotic figure is observed. A moderate amount of fibrous stroma permeates between the cells; the vascular tree is not readily evident. The second and more interesting component is made up of nests of small cells that have scant cytoplasm that may be vacuolated, a small nucleus containing many small chromatin granules and, rarely, a small basophilic

[2] Biskind, G. R., and Mark, J., *Bull. Johns Hopkins Hosp.*, 1939, **65**, 212.

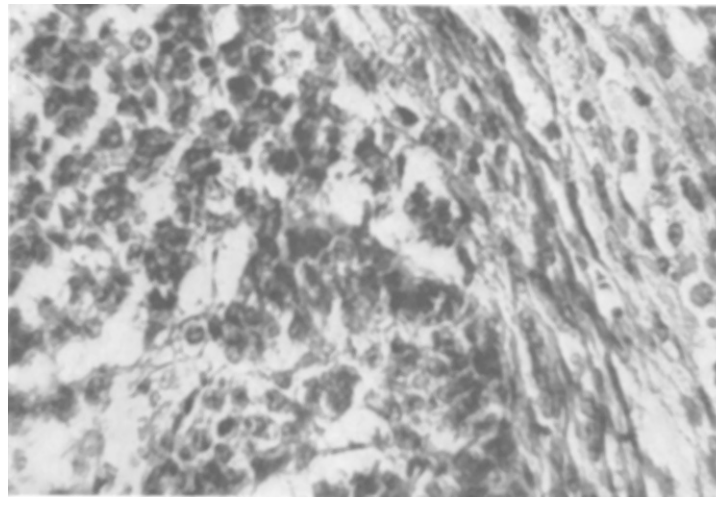

FIG. 2.
"Granulosa" cells and adjacent interstitial cells (about 240 ×).

nucleolus. Mitotic figures are fairly numerous. These nests often have a limiting fibrous strand and the cells are retracted from the strand in many places leaving irregular vacuoles. These small cells may be arranged in compact masses that sometimes take on a poorly developed adenomatous or papillary pattern. Small cysts are formed that may contain a pink staining coagulum. In several places there is an intermingling of the large cells and the nests of small cells. In addition to this intermingling, in many places there are minute nests of small cells entirely surrounded by the large cells. These minute collections are slightly larger than those of the spermatic tubules but are highly suggestive of a tubular origin, and are reminiscent of the pattern seen in arrhenoblastoma (Fig. 3). At one point there are small remnants of epididymis and some atrophic spermatic tubules. The splenic substance is not altered except for evidences of old hemorrhage around the fibrous capsule of the tumor.

Another implant, observed after 11 months, is made up of fairly well preserved epididymal tubules and many atrophic spermatic tubules lying in a mass of large cells that must be derived from the interstitial cells. There is a slight increase in fibrous stroma between these cells, and in one place there is a deposit of basophilic granular material, probably calcium. The spermatic tubules are shrunken and empty except for a single layer of small vacuolated cells that have a pyknotic nucleus; this appearance is quite characteristic of the atrophy that occurs in maldescent of the testis.

A third implant, 11 months after insertion in the spleen, has a histologic structure quite similar to that of the mass just described, except that there is a greater proliferation of the interstitial elements and fewer tubules. In some regions the interstitial cells have a distinct granular cytoplasm; in other places most of the cells are vacuolated. There are many more vascular channels in this interstitial cell mass.

A fourth implant observed at 9 months is also of interest. The tubules have not undergone as extensive atrophy; some are lined by 1, 2, or 3 layers of cells. The row of cells that rests on the basement membrane is made up of larger cells, with vacuolated cytoplasm and somewhat vesicular nucleus. The upper rows are composed of smaller cells, poorly defined, that have a small round nucleus in which the chromatin is often placed in threads; these are remnants of the spermatogenic elements. In some of the degenerating tubules these cells appear piled up in one segment of the tubule, in which the basement membrane has disappeared, suggesting beginning invasion of the interstitial cell mass by tubular cells.

One of the most striking features of the

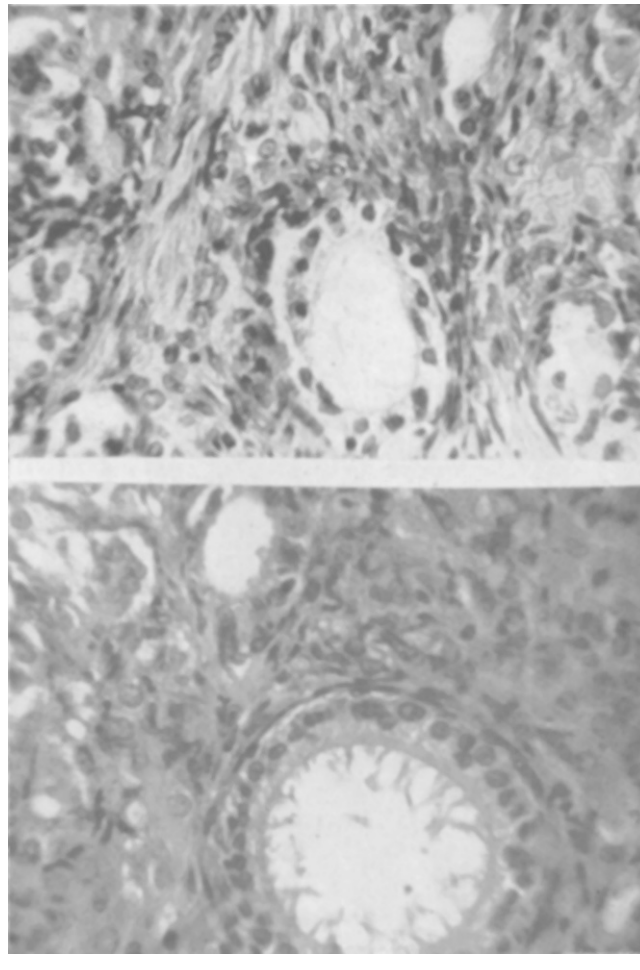

FIG. 3.
Arrhenoblastoma-like structures in interstitial cell mass (about 240 ×).

large tumor described (Fig. 1 to 3) is the resemblance of each of the two components, the small cells lying in irregular nests and the large cells arranged in sheets, to the two components observed in the tumors of the ovary produced by this method.[1] Not only is there a striking similarity of the small cells of the testicular tumor to the granulosa cells of the ovarian tumor, but even the interstitial cells of the testicular tumor closely resemble the theca elements of the other. In fact, were it not for the epididymal remnants, these two different tumors might be indistinguishable.†

Summary. The fact that estrogens and androgens are inactivated in the liver, served as the basis for studies on the effect of transplantation of the gonads to the spleen, which is in the portal circulation. Hepatic destruction of the gonadal steroids removes their normal inhibiting influence on the pituitary, permitting excessive secretion of gonadotrophin.

Implantation of the testis of an infantile rat into the spleen of an adult male castrate, resulted after 11 months in the development of a large tumor, bearing a striking resemblance to the granulosa cell tumor of the ovary

† We are indebted to Dr. Alfred Plaut and his staff for preparation of the histologic sections of the testicular implants.

produced by a similar method, previously reported. The cellular component apparently derived from the tubules and the interstitial cell mass in the testicular tumor, are indistinguishable from the granulosa cell and theca cell components, respectively, of the ovarian tumor. In addition, certain portions of the testicular tumor are reminiscent of the structure seen in arrhenoblastoma.

14959 P

The Cause of Epidemic Diarrhea, Nausea and Vomiting. (Viral Dysentery?)

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Tests were made to discover if the disease called epidemic nausea, vomiting and diarrhea[1] or infectious gastroenteritis is (a) caused by a filtrable agent and (b) transmitted as an airborne disease; (c) if the portal of entry is the respiratory tract or the gastrointestinal tract and (d) whether the causative agent is present in the oropharynx, intestine, or blood.

The experiments were made on medical student volunteers under conditions not best suited to work of this kind. The students for obvious reasons could not be segregated, the number of test subjects was limited, and since the material obtained from patients with the disease was immediately filtered and given to volunteers, the experiments were made during a declining natural epidemic. The tests were begun about 3 weeks after the peak of the epidemic[1] had passed and while only 1 or 2 remnant attacks occurred daily or at intervals of days.

Broth garglings and suspensions of diarrheal stool samples were filtered through medium Mandler filters, nebulized and applied to volunteers usually within a period of 2 to 4 hours after their collection. Bacteria-free filtrates were nebulized in Wells flasks[2] with compressed air, and could be seen by transmitted light emerging from the flasks as a fine, almost imperceptible mist. The stream was directed into a large pasteboard box into which the volunteer's head was placed for 5 minutes. Volunteers and the rest of the student body were then questioned at short intervals for 3 weeks for the development of symptoms.

Thirty-two volunteers in sets of about 8 on different days inhaled filtrates of garglings; of these 17 had attacks from 1 to 21 days afterward, mostly between 1 and 4 days. The symptoms reported were malaise, headache, abdominal discomfort, nausea, vomiting and diarrhea in varying combinations and in varying severity, mostly mild. In 7, mild nasopharyngitis occurred in addition.

Twenty-one volunteers inhaled stool filtrates and, of these, 11 developed similar symptoms in a similar period, 3 with mild nasopharyngitis also. No symptoms developed in 6 who inhaled nebulized serum.

Fifteen volunteers swallowed 3 cc of filtered garglings enclosed in double gelatin capsules, 5 swallowed stool filtrates, and 4 swallowed serum each similarly encapsulated. No significant symptoms developed in any.

In the remainder of the 240 students in the classes from which the volunteers were drawn, 22 attacks apparently of the declining epidemic disease occurred during the 4-week period while the experiments were in progress, as shown in Fig. 1. Some of these may have been contracted from ambulatory, sick volunteers.

Summary. Among the 32 volunteers who inhaled nebulized filtered garglings, symptoms developed in 17; of the 21 who inhaled nebu-

[1] Reimann, H. A., Hodges, J. H., and Price, A. H., *J. A. M. A.*, 1945, **127**, 1; Reimann, H. A., Price, A. H., and Hodges, J. H., PROC. SOC. EXP. BIOL. AND MED., 1944, **55**, 233.

[2] Wells, W. F., to be published.