TABLE I.
Duration and Height of Fever and Jaundice and Severity of Illness in 5 Human Volunteers with Experimentally Induced Infectious Hepatitis.

Volunteer	Inoculum	Source*	Amt cc	Route	Duration days: Incub. per.	Duration days: Fever	Duration days: Jaundice	Maximum: Fever†	Maximum: Serum Bilirubin mg. %	Severity
BS	S	3-7th day disease (8 patients)	0.5	P	27	13	13	103.8	7.6	++
TR	S	"	0.5	P	28	5	14	101.0	2.5	+
SR	F	"	10	O	27	12	30	104.0	7.0	+++
HD	F	"	10	O	17	5	22	100.5	7.3	++
FW	F	"	10	O	15	10	14	102.5	7.4	++

S = Serum; F = Feces; P = Parenteral; O = Oral.
* Cf. Fig. 1. † Rectal temperatures are recorded.
Feces were administered as Seitz filtrates of 10% suspensions.

Three volunteers were fed the stool filtrate and 3 were inoculated sub- and intracutaneously with serum. The results are indicated in Fig. 1. It is apparent that virus is present in both the stool and serum of patients in the acute-phase of *parenterally induced* infectious hepatitis. Certain clinical data on the 5 volunteers who contracted the disease in this experiment are recorded in Table I.

Summary. 1. A strain of infectious hepatitis virus inoculated *parenterally* into 8 human volunteers was recovered from pools of serum and feces obtained from these same subjects during the acute-phase of their illness. These materials produced infectious hepatitis in 5 out of 6 healthy, human volunteers on reinoculation.

2. This recovery of virus from the stool of patients with infectious hepatitis induced by *parenteral inoculation* constitutes an apparent difference between this condition and homologous serum jaundice in which the etiologic agent has not been recovered from the stool up to the present time.

15277 P

Transplantability of Induced Granulosa Cell Tumors and of Luteoma in Mice. Secondary Effects of These Growths.*

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Granulosa cell tumors can be readily induced in the ovaries of mice by exposing the latter to X-rays.[1-3] A single dose of 87r given over the entire body to 44 mice approximately 6 weeks of age produced tumors in 31 mice. The induced ovarian growths

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1 Furth, J., and Furth, O. B., *Am. J. Cancer,* 1936, **28**, 54.

2 Furth, J., and Butterworth, J. S., *Am. J. Cancer,* 1936, **28**, 66.

3 Geist, S. H., Gaines, J. H., and Pollack, A. D., *Am. J. Obs. and Gyn.,* 1939, **38**, 786.

TABLE I.

	Males		Females		Total	
	Implanted	+	Implanted	+	Implanted	+
F1 mice						
Normal	23	11	21	8	44	19
X-rayed	5	1	20	12	25	13
Gonadectomized	10	8	15	12	25	20
Total	38	20	56	32	94	52
Parental (AK or Rf mice)	25	0	11	0	36	0

were of 3 main histological types: (a) tubular adenomas, (b) granulosa cell tumors, and (c) luteomas. The microscopic characteristics of these tumors have already been described and illustrated.[2]

Of 21 attempts at transfer of induced ovarian tumors, 13 proved successful. Induced tubular adenomas of 3 mice were successfully transplanted but only one has been carried in serial passages. This is a very slow growing tumor, becoming palpable (about 2 mm in size) after approximately 6 months (Strain VI). Two induced luteomas proved readily transplantable (Strains IX and XI). Cells of luteomata proliferate by mitotic division retaining the morphological characteristics of lutein cells in mice of both sexes. Mice bearing luteoma of Strain IX do not show evidence of hyperestrinization; the adrenal cortices undergo profound atrophy. These mice gained much weight, mainly by excessive deposition of fat in the normal fat depots.

The other transplantable ovarian tumors are granulosa cell growths. Strain I recently described[4] produces a cavernous dilatation of the liver sinusoids with only occasional secondary parenchymal damage which led to the suggestion that abnormal steroids may have been produced by the tumor and metabolized in the liver.[4]

Granulosa cell carcinoma, Strain III, now to be described, originated in an F1† mouse that had been given 175r at an age of 6 weeks and was subsequently painted with 0.5 percent methylcholanthrene dissolved in benzene (cf.[5]). Nine months after the irradiation a tumor felt at the site of the left ovary was removed and fragments of it were implanted into the subcutaneous tissue of this and 10 other F1 mice. When the donor animal died 7 weeks later the transplant measured 2x2x1 cm and the lung contained metastatic ovarian carcinoma.

The results of 9 subsequent transplantation experiments (4 successive passages) are summarized in Table I.

These figures indicate that the range of transmissibility of these ovarian tumor cells resembles closely that of normal cells (cf.[5]). At first the tumors grew slowly, becoming palpable only after about 4 months; but later their growth vigor increased and they became palpable within 6 to 8 weeks after transplantation. Metastases occurred in the liver and lungs.

The histological character of the tumor remained unaltered throughout the course of these passages. The tumors are composed of small granulosa-like cells which do not form follicles. They are widely separated by some pale staining material, perhaps their secretion. Necrosis with secondary calcification is common in the tumors and in such areas fibroblast-like cells can be seen which contain alkaline phosphatase granules in abundance and occasionally there is ossification.

There is continued estrus in most spayed or normal female mice bearing large tumors of Strain III, while in male mice the testes and seminal vesicles undergo profound atrophy. The thymus is markedly atrophic

[4] Furth, J., and Boon, M. C., PROC. SOC. EXP. BIOL. AND MED., 1945, **58**, 112.

† Rf × AK hybrid.

[5] Furth, J., and Boon, M. C., *Science*, 1943, **98**, 138.

in all tumor-bearing mice. In a few mice osteosclerosis of the femor, similar to that produced by estrogenic hormones[7] is noted. In addition, most, if not all, mice with large transmitted tumors had a cavernous dilatation of the sinusoids of the liver, spleen and adrenals. The weight of the liver was approximately 3 times normal in many mice, accounted for almost exclusively by an increment of blood. Although blood volume determinations have thus far not been made, the observations made suggest a marked rise in blood volume in mice exhibiting the liver change described. The cavernous dilatation of vessels was localized to viscera of the abdomen named. The vessels leading to the grafted tumor were also tremendously distended.

The mouse in which Strain III originated received both X-rays and methylcholanthrene. Extensive experience has shown that the latter alone does not produce ovarian tumors while X-rays alone have done so in almost as high a percentage of the mice as the combined treatment with X-rays and methylcholanthrene. However, a preliminary tabulation of our data shows that in mice receiving the combined treatment the tumors were larger, appeared sooner, were more readily transmissible and more apt to metastasize than those receiving X-rays only. In the latter, most tumors were of the tubular adenoma type, presumably derived from downgrowth of the germinal epithelium, while in the former, most tumors were of the granulosa or lutein cell types.

Summary. Eleven ovarian tumors, induced by X-rays have been transmitted in successive passages. Eight were of the granulosa cell types, 2 were luteomas and one was a tubular adenoma. Histological changes indicate that cells of Strain III secrete estrogens. Mice bearing tumors of this strain also have a cavernous dilatation of the sinusoids of liver, spleen and adrenals. In mice bearing large luteoma of Strain IX there is profound atrophy of the adrenal cortex.

6 Kaliss, N., and Robertson, T., *Genetics*, 1943, **28**, 78.

7 Gardner, W. U., and Pfeiffer, C. A., PROC. SOC. EXP. BIOL. AND MED., 1938, **37**, 678.

15278

A Method for Detection of Streptothricin in the Presence of Streptomycin.

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Streptomycin[1] and streptothricin,[2] two antibiotic agents having almost identical bacterial spectra,[3,4] are both produced by members of the actinomycetes, namely, *Actinomyces griseus* and *Actinomyces lavendulae* respectively. Because of this close relationship and of the still existing difficulty in the identification of the various members of the actinomycetes,[5] it is possible that strains of the organisms producing these 2 antibiotics might be confused. Such a confusion would be particularly undesirable when it is recognized that streptothricin is many times more toxic than streptomycin and in addition, has a distinct delayed toxicity.[6,7] Streptomycin,

1 Schatz, A., Bugie, E., and Waksman, S. A., PROC. SOC. EXP. BIOL. AND MED., 1944, **55**, 66.

2 Waksman, S. A., and Woodruff, H. B., PROC. SOC. EXP. BIOL. AND MED., 1942, **49**, 207.

3 Robinson, H. J., Smith, D. G., and Graessle, O. E., PROC. SOC. EXP. BIOL. AND MED., 1944, **57**, 226.

4 Robinson, H. J., Graessle, O. E., and Smith, D. G., *Science*, 1944, **99**, 540.

5 Waksman, S. A., and Henrici, A. T., *J. Bact.*, 1943, **46**, 337.

6 Rake, G., Hamre, D., Kavanagh, F., Koerber, W. L., and Donovich, R., *Am. J. Med. Sc.*, 1945, **210**, 61.

7 Robinson, H. J., Graessle, O. E., Gundel, M., and Silber, R. H., in press.