injected twice daily—mostly intraperitoneally, but subcutaneously when the health of the animals became affected—from March 22 to April 15 inclusive; 25 days in all. The accompanying chart illustrates the growth of the treated and untreated tumours. A glance at it shows that Mr. Thompson's extract has not inhibited the growth of the tumours; there is no difference beyond chance variation between the treated and untreated animals. In this experiment the lack of "growth-inhibitory" power became evident very early; for in spite of injections being started before palpable tumours had appeared and when the amount of living tumour tissue could not have been more than 0.02 c.cm. — the volume of the original inoculum—measurable tumours equal to those in the control mice were present after 8 days of treatment. These continued to grow normally, as the chart shows. The sizes attained by the tumours can be gauged by the weight of tumour in Mouse 1 of the chart on April 15; it was weighed after removal, and equalled 9.9 g.

Paris R 111 strain of inbred mice grafted with mouse carcinoma 63 on March 18, 1943. Mice 1 to 6, inclusive, treated with 80 K. Injections were begun on March 22, and were continued daily to April 15.

The results of tests on tissue cultures were also negative. The tumours used were carcinomas No. 63 and Strong A, and C 57 sarcoma; the normal tissues used for comparison were embryo heart fibroblasts and embryo kidney. In experiments in which H 11, in a final concentration of about 1 to 4, was added to 3-day-old cultures in active growth there was no detectable influence on the normal or malignant cells. When the urine extract was added to the medium immediately the tissues were explanted, it was found that in final dilutions of 1 in 2 normal and malignant cells were killed equally; in dilutions of 1 in 10 growth was equal in normal and malignant cells. No specific inhibition of growth of tumour cells was observed.

From the results of these investigations we conclude that H 11 has no "growth-inhibitory" effects on the tumours used in the experiments.

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OBSERVATIONS ON THE USE OF H 11 IN CARCINOMA

BY

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During the past two years an increasing number of workers have described growth-inhibiting properties of urinary extracts. Turner (1939) indicated an inhibiting effect from an alcoholic fraction of urine, while Bowman and Mottshaw (1941) studied the growth-inhibiting properties of a similar extract on tumour growth. Other workers include Rohdenburg and Nagy (1937) and Murlin *et al.* (1939), who claimed anticarcinogenic properties for such extracts. Thompson *et al.* (1941) published a preliminary account of the preparation of an alcoholic fraction of urine named H 11, and described not only its biological properties and anticarcinogenic action in transplanted animal tumours but also the inhibitory effect on human cancer.

The Present Investigation

An investigation into the effect of H 11 extract on carcinoma was begun at the Kingston County Hospital in Oct., 1940, and it is now thought advisable to issue an interim report, although no conclusions can be drawn, as the cases have not been followed up for a sufficient period.

Of the 51 advanced cases 14 received insufficient treatment, and of the remaining 37 patients 11 are dead and no reply was received from 5. Of the 21 patients known to be alive 4 have been under observation for under one year, 12 for over

one year, and 5 for over eighteen months. All the surviving cases except two received some other form of therapy, and in these two—Nos. 18 and 38—the diagnosis was not confirmed, as biopsy could not be performed.

The series (see Table) contains different types of carcinoma situated in various parts of the body. In most instances the condition was inoperable, and usually the patient was in poor general health, although there was considered to be a sufficiently reasonable expectation of life to justify treatment. This period of time was assessed at six weeks in accordance with the statement made by Thompson that objective signs of improvement do not usually occur until such an interval of treatment has elapsed. Some cases had other treatment, including operation and radium, but with few exceptions they were cases in which the operation or radium therapy was considered to be insufficient to eradicate the local disease.

There is some evidence that in a few cases the rate of growth has been slowed up or inhibited, but in no case confirmed by section has, as yet, any growth disappeared as the result of H 11 therapy only. Further research is essential in order to purify the extract, and a more satisfactory method of dosage must be evolved so as to keep the concentration in the blood at a constant level.

No case of carcinoma should be treated by H 11 alone unless a competent surgeon has advised that it is inoperable and unsuitable for radiotherapy, etc. Treatment must be given for at least six months, and the cost should be carefully considered before advising or starting this form of therapy.

H 11 extract has been supplied for this investigation by the generosity of Standard Laboratories, who have prepared the extract. All the research and experimental work has been carried out at the Hosa Research Laboratories by the Director of Research, Mr. J. H. Thompson, and his staff.

Case	Age and Sex	Date of First Injec.	Pathology	Previous Treatment	No. of H 11 Injec.	Result of Examination April, 1942	Result of Examination October, 1942
1	F 57	7/10/41	Infil. left broad lig.; col- lapsed carc. vagina	Radium	63	Less pain. Died 3/1/42	
2	F 35	19/2/42	Adenocarc. breast; sec. lungs and retina	—	496	Less pain; growths sta- tionary	Wt. 9 st. Pain back and shoulders. Totally blind. Can get about, but becom- ing weaker
3	F 39	4/3/41	Solid trabecular polygonal carc. cervix, Grade III	Radium	24, irreg.	Died Sept., 1941	
4	F 61	17/2/41	Carc. cervix, Grade III	Radium; hysterectomy; pre-sacral; neurectomy	950	G.C. v. good 1/5/42. N.A.D. per rectum, vagina, and pelvis; no pain, no dis- charge	G.C. good; rather pale; no pain or discharge; work- ing full day; wt. 9 st., stationary. P.R., utero- sacral thickened
5	F 46	21/5/41	Squamous carc. cervix, Grade III-IV	Pre-sacral neurectomy; radium	22, irreg.	Died 2/12/41	
6	F 53	7/6/41	Squamous carc. cervix, Grade III	Radium; pre-sacral neur- ectomy	20, irreg.	Died 16/8/41	
7	F 56	11/2/41	Solid trabecular poly- gonal and cubical carc. uterus	Radium; subtotal hyster- ectomy	120	Died 21/12/41	
8	M 69	11/7/41	Carc. prostate; renal calculi	Suprapubic cystotomy	30, irreg.	Died 6/9/41	
9	M 20	7/1/42	Mucus-secreting carc. rectum	Colostomy	62, irreg.	Died 10/3/42	
10	F 46	7/1/42	Mammary carc.; spastic paraplegia	—	31, once daily	Return of sensation in lower limbs, 19/3/42. Died 28/4/42	
11	F 56	6/10/40	Papillary carc.; cyst ovary; sec. in peritoneum	Total hysterectomy	119, irreg.	G.C. v. good; no pain, no ascites	Letter states now well. No symptoms
12	F 46	18/3/41	Carc. stomach and ovary	—	10	Died 27/3/41	
13	M 55	26/2/41	Carc. stomach	—	21	G.C. fair; no vomiting	Dead
14	F 60	21/8/40	Carc. uterus	Total hysterectomy; supra- pubic cystotomy	84, once daily	Died 10/2/41	
15	M 68	10/10/40	Carc. stomach and lower end oesophagus	Gastrostomy	22, irreg.	i.s.q.	No reply
16	M 70	18/12/41	Columnar carc. stomach	—	120, irreg.	Died 25/2/42	
17	F 51	July, 1941	Malignant ovarian; numer- ous small metastases; ascites	Laparotomy; left oophor- ectomy	520	N.A.D. abdomen or pelvis. G.C. v. good; gaining weight; no pain, no ascites	G.C. good; no pain or symp- toms. Injections stopped in March. No signs of re- currence. Gaining weight
18	F 60	Oct., 1940	Carc. rectum; sec. liver. Not confirmed by section	Laparotomy	460	N.A.D. per rectum except slt. thickening of recto- vaginal septum. G.C. very good	Very well; no symptoms or abnormal physical signs
19	M 72	Feb., 1941	Carc. rectum	Colostomy	650	Growth now involving anus. Wt. constant; G.C. i.s.q.	Gets about, but G.C. poor and pain+. Refused further injections; growth extending.
20	F 56	Dec., 1941	Carc. cervix, Grade III	Radium; pre-sacral neur- ectomy	186	No ulcer, no pain, no haemorrhage; gain in wt.; G.C. imp.	G.C. good; wt. 12 st. 6½ lb.; no symptoms or signs of recurrence
21	F 68	Dec., 1941	Carc. vagina	Colostomy; pre-sacral neurectomy; rt. int. iliac ligatured	182	G.C. improved, less dis- charge; losing weight. Died 18/6/42	
22	F 60	May, 1941	Transitional carc. cervix, Grade III	Radium; pre-sacral neur- ectomy	380	G.C. good; gaining weight; no pain	G.C. v. good; wt. 11 st. 13 lb.; no pain or symp- toms, slight thickening of rt. utero-sacral lig.
23	M 63	July, 1941	Cylindroma of salivary glands	—	248	Mass of glands in neck enlarging	Dead
24	F 53	Jan., 1942	Solid trabecular transi- tional and squamous carc. cervix, Grade III	Radium; laparotomy; pre- sacral neurectomy	188	N.A.D. in abdomen. G.C. v. good; no discharge, no haemorrhage; gain- ing weight	No reply
25	F 45	June, 1941	Squamous and prick- lelled carc. uteri, Grade III	Radium; subtotal hyster- ectomy; colostomy	1,116	No pain; gain wt.; N.A.D. in pelvis; G.C. very good	G.C. v. good; wt. increas- ing; no symptoms or signs of recurrence. Col- ostomy to be closed.
26	M 66	Mar., 1941	Carc. bronchus	—	730	Pain relieved for a time. Mass in neck now ulcer- ated through skin	Dead
27	F 53	May, 1941	Solid trabecular poly- gonal and transitional carc. cervix	Radium; Wertheim's hys- terectomy; pre-sacral neurectomy	744	No pain; no discharge; N.A.D. in abdomen. G.C. impd.; gain in wt. Vesico-vaginal fistula from radium necrosis	G.C. good; wt. increasing. 9 st. 12 lb. No recurrence. Has vesico-vaginal fistula, some thickening of rt. utero-sacral lig.
28	F 79	Apr., 1941	Transitional and squamous trabecular carc. cervix, Grade III	Radium	616	Less pain. Died Dec., 1941	
29	F 75	June, 1941	Malignant melanoma of neck	Local excision	342	No recurrence. Two months after discontinu- ing H 11 small gland appeared. Block dis- section April, 1942	G.C. fair; wt. 8 st. 8 lb., increasing. Some pain in shoulder, but x-ray N.A.D. and no signs of recurrence
30	M 44	20/4/41	Carc. rectum; metastases in abdominal and in- guinal glands	Colostomy	153	Primary growth i.s.q.; in- guinal glands smaller. G.C. good; gain in weight. Died 25/4/42	
31	F 58	Sept., 1941	Solid trabecular and squam- ous carc. cervix, Grade III	Radium; pre-sacral neur- ectomy	424	No pain, no discharge; gain wt. G.C. v. good	No pain or discharge. Still having 5 c.cm. daily
32	F 39	Feb., 1942	Gastric carc.	Laparotomy	220	Little pain; G.C. fair; vomiting	Now complains of pain and vomiting, and has abdomi- nal tumour, probably Krukenberg
33	M 68	27/6/41	Carc. prostate	—	538	25/4/42: Prostate i.s.q.; has retention of urine; G.C. satisfactory	No reply
34	M 70	Dec., 1941	Columnar carc. prostate; mass in left lung	Deep x-ray	58	Died Feb., 1942	
35	F 62	Jan., 1942	Carc. cervix	Radium; pre-sacral neur- ectomy	98	Died 9/3/42	
36	F 56	Sept., 1941	Squamous prickled and horny carc. cervix, Grade III	Radium	256	Repeat radium March, 1942. Growth checked; G.C. impd.; gain in wt.; no discharge, pain, or incontinence. Died 28/4/42	
37	F 66	July, 1941	Squamous carc. cervix, Grade II-IV	Radium; diathermy	1,116	No pain; G.C. satis. N.A.D. in abdomen; utero-sacral lig. still thickened	G.C. v. good; wt. 14 st. 4 lb., increasing; no symptoms; no signs of recurrence, but some thickening of both utero-sacral lig. In- jections now stopped

Case	Age and Sex	Date of First Injec.	Pathology	Previous Treatment	No. of H 11 Injec.	Result of Examination April, 1942	Result of Examination October, 1942
38	M 53	June, 1941	Carc. prostate; not confirmed by section	—	620	Gland normal; gain in wt.; G.C. v. good; micturition normal	G.C. v. good; no symptoms; no nocturnal frequency. P.R., prostate soft; rt. lobe +
39	F 58	Oct., 1941	Squamous carc. cervix, Grade III	Radium	744	No discharge, no symptoms, no pain; G.C. impd. 22/4/42	G.C. v. good; wt. increasing, 7 st. 13 lb.; no pain or symptoms; no signs of recurrence. Injections now stopped
40	F 47	July, 1941	Squamous carc. of cervical stump; had hysterectomy several years previously for fibroids. Large ulcerating mass	Radium; pre-sacral neurectomy	558	V. sat. condition; some scarring vaginal walls; no pain; a little loss of wt.	G.C. v. good; lost 10 lb. in wt. since April; has thickening rt. utero-sacral lig. and small mass in pelvis. To have further injections
41	F 45	Aug., 1941	Squamous carc. cervix, Grade III	Radium; pre-sacral neurectomy; Wertheim's hysterectomy	558	N.A.D. abdomen; no pain; G.C. v. good; scarring and a little thickening of vaginal vault	G.C. v. good; wt. 11 st. 6 lb. Injections stopped in April, 1942. No symptoms; P.R., both utero-sacral thickened
42	F 47	Sept., 1941	Carcinoma cervix, Grade IV	Radium	447	N.A.D. abdomen; no haemorrhage; no discharge; G.C. v. good. P.V., scarred cervix	Gradually lost wt. and pain recurred. Died 11/8/42
43	F 56	Oct., 1941	Solid trabecular transitional and squamous carc. cervix	Radium; pre-sacral neurectomy	249	G.C. v. sat.; gain in wt., 10 st. 7 lb.; no pain; slight cervical scarring	G.C. good; wt. 11 st. 2 lb.; no symptoms but tiredness; utero-sacral ligaments thickened. To have further injections
44	M 60	Sept., 1941	Carc. prostate	—	98, irreg.	—	Doctor states G.C. good; wt. stationary; no pain; working, and feels well
45	M 21	Jan., 1942	Carc. rectum	—	188	Died	Died
46	F 46	Jan., 1942	Carc. cervix	Radium	150	Condition worse	No reply
47	F 26	30/10/41	Carc. stomach	Gastrectomy	240	27/2/42; Epigastric tumour; G.C. deteriorating; losing wt.; vomiting+	
48	F 60	13/1/41	Carc. uterus	Wertheim's and radium, followed by recurrence and suprapubic cystotomy	200	No improvement. Died 10/2/42	
49	F 70	9/10/41	Carc. cervix, Grade II	Radium	300	22/4/42: Satis.; G.C. good; no secs. palpable	Dead
50	F 29	1/11/40	Carc. ovary	Ovariectomy; glands +	19, stopped at patient's request	V. rapid growth, causing intestinal obst. Died 19/12/40 ? accelerated by withdrawal of growth-inhibiting factor	
51	F 60	28/8/41	Carc. breast (scirrhus)	Nil; patient refused operation or radiotherapy	540, irreg.	19/6/42: Operable. Growth slowly increasing: started approx. 1" in diameter, now 1½"	No reply

I wish to express my thanks to the medical and nursing staff of the Kingston County Hospital for their assistance, and to the general practitioners who have co-operated in giving the injections to the patients in their own homes. In particular I am indebted to Mr. J. V. O'Sullivan for his great interest in this research and for his valuable suggestions.

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CUTANEOUS HYPERSENSITIVITY TO SULPHONAMIDES

A REPORT OF 12 CASES

BY

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The following cases illustrate a type of sulphonamide eruption which is being recognized with increasing frequency in the Middle East, but to which I am unable to find any reference in the literature at my disposal. In a previous report from this hospital on sulphonamide eruptions of the photosensitive type (Park and Platts, 1942) it was pointed out that these rashes almost invariably begin after 7 to 10 days of sulphonamide therapy, when there is presumably a high concentration of the drug in the blood. One case, however, was quoted in which there was a severe dermatitis beginning immediately after the first doses of sulphanilamide, differing from the delayed eruptions in its exudative character. An analogy was drawn between this condition and the experimental observations of Epstein (1939), who obtained erythematous and exudative reactions respectively to ultra-violet irradiation of the sites

of two successive injections of sulphanilamide, nine days apart. This phenomenon he christened "photo-allergy." The cases reported below are all of the immediate type, some of the generalized ones being unmistakably photosensitive, and it has been found that all of them have had sulphonamides applied to the skin some time before their eruptions.

Case I

On Aug. 16, 1942, Private B., aged 36, developed a seborrhoeic intertrigo of the left axilla. On the 19th this became pustular, and sulphanilamide ointment was applied, clearing up the secondary infection and leaving the intertrigo as before. He gave a history of a widespread eruption, lasting several weeks, following sulphanilamide dressings to a wound of the back 8 months previously. On Aug. 23 he developed acute tonsillitis, and was given three 0.5-g. doses of sulphanilamide by mouth. That evening the intertrigo became worse and a general rash appeared.

Next day, on admission to hospital, he showed a weeping eczematous intertrigo of the axilla and a diffuse papular dermatitis of the trunk and limbs. He received no more sulphanilamide until Sept. 1, when his tonsillitis recurred. Three 4-hourly doses of 1 g. were then given, and that evening the entire eruption recurred, more severely than the first time. It took two weeks to clear. On Sept. 23 0.5 g. of sulphapyridine caused a mild erythematous reaction at all the previous a.e.s., lasting two days. On Sept. 26 1 g. of sulphaguanidine produced no reaction. On the 27th 5 g. of sulphaguanidine gave a mild erythematous reaction. On Oct. 1 1.5 g. of sulphathiazole caused no reaction.

On Oct. 4 a paste consisting of equal parts of sulphanilamide, starch, soft paraffin, and lanolin was applied to several test areas. This caused an immediate reaction in the left axilla, but none on any other part of the skin. Intradermal tests were carried out with 0.01, 0.1, and 1% of sulphanilamide in normal saline, using controls of normal saline alone. Only the 1% gave a reaction, consisting of a raised erythema, beginning in about 4 hours and lasting 24 hours.

Case II

On Aug. 1, 1942, Leading Aircraftman T., aged 38, suffered abrasions of the left elbow which became infected and were treated with eusol and sulphanilamide, applied locally. On Aug. 8 an