

In order that the biologic activities which have been indicated for the anti-microsomal antibody not be assigned to an antithyroglobulin response, the following statements as based upon experimental data can be made. Although the well-washed microsomes can be shown to have a thyroglobulin contaminant with guinea pig antithyroglobulin antiserum, rabbits immunized with the microsomes initially developed low levels of antithyroglobulin titers as measured by passive hemagglutination, with a subsequent rise in titer late in the disease (maximum, 1:256), whereas the antimicrosomal antibody appeared early and in high titer. Moreover, as indicated in the absorption studies, thyroglobulin did not remove the stated properties of the antibody. Finally, 20 mg of thyroglobulin protein was required to induce a milder form of thyroiditis as compared to 10 mg of microsomal protein which induced the described severe disease.

The foregoing data establish two main features of experimental thyroiditis never before reported: (i) the induction of severe chronic thyroiditis in nonprimate mammals with homologous microsomal immunization, and (ii) the concomitant production of a circulating antimicrosomal antibody.

As to why this laboratory has been successful in achieving microsome-induced thyroiditis and antimicrosomal

antibody in a nonprimate mammal whereas others have failed is not too easily dissected. However, as possible reasons the following are presented: (i) break in tolerance by the extremely large pool size of thyroids for microsomal isolation; (ii) the use of freshly isolated microsomal material for each injection (frozen thyroids were ineffectual for these experiments); and (iii) electron microscopic evaluation of each preparation prior to use and discard of unsatisfactory ones.

MARAYART MANGKORNKANOK

A. S. MARKOWITZ

HECTOR A. BATTIFORA

Department of Microbiology,

University of Illinois at the Medical

Center, Chicago, Hektoen Institute

for Medical Research of Cook County

Hospital, Chicago, and Department of

Pathology, Wesley Memorial Hospital,

Chicago, Illinois

References and Notes

1. H. E. H. Jones and I. M. Roitt, *Brit. J. Exp. Pathol.* **42**, 564 (1961).
2. I. M. Roitt, N. R. Ling, D. Doniach, K. G. Couchman, *Immunology* **7**, 375 (1964).
3. J. H. Kite, Jr., H. Argue, N. R. Rose, *Clin. Exp. Immunol.* **1**, 139 (1966).
4. P. N. Campbell and B. A. Kernot, *Biochem. J.* **82**, 262 (1962).
5. Details concerning the disease are in preparation.
6. Address all correspondence and reprint requests to A. S. Markowitz, Hektoen Institute for Medical Research, 627 S. Wood St., Chicago, Ill. 60612.
7. Presented in part for the degree of doctor of philosophy, University of Illinois at the Medical Center, by M.M.

26 May 1972

Herpesvirus Type 2 in the Male Genitourinary Tract

Abstract. *A population study of 190 randomly selected male patients with no history of genital herpesvirus infection revealed a high incidence of herpesvirus type 2 in genitourinary specimens. This indicates that men serve as a reservoir of genital herpesvirus.*

Epidemiologic studies indicate that genital herpes (herpesvirus type 2) is venereally transmitted (1). Antibodies to herpesvirus type 2 are associated with early and vigorous sexual activity and promiscuity, and are more common in prostitutes than in a control population (2).

A strong association exists between antibodies to herpesvirus type 2 and cervical neoplasia. The evidence, although circumstantial and sometimes conflicting, is based on the higher frequency and titer of antibodies to herpesvirus type 2 found in patients with carcinoma of the cervix than in matched populations without evidence of cervical cancer (3). In addition, Aurelian

(4) reported the isolation of herpesvirus type 2 from a cervical carcinoma grown in culture, and Duff *et al.* (5) reported the oncogenic transformation of hamster cells exposed to a strain of irradiated herpesvirus type 2. Such cells

Table 1. Distribution, according to age groups, of cultures positive for herpesvirus.

Age group (years)	Positive cultures (No.)	Men (No.)	Positive for age group (%)
70+	7	46	15.2
60 to 70	5	28	17.9
45 to 60	6	41	14.6
15 to 45	9	68	13.2

were able to produce tumors in newborn hamsters.

A previous survey of a population of upper-middle-class women revealed an extremely low incidence of recovery of virus from the genital tract (6). The present study was undertaken to determine whether the male genitourinary tract could be a reservoir of herpesvirus.

Over a period of 5 months 190 male patients were randomly selected from the University of Florida Urology Clinic; they ranged in age from 15 to 85 years, represented virtually the entire gamut of socioeconomic classes, and were of mixed racial composition. Subjects had no previous history of genital herpesvirus infection.

Specimens collected included urethral swabs, prostate fluid, sections of vas deferens removed during procedures for sterilization, prostate biopsies, and miscellaneous samples such as testicular biopsies and foreskin tissue. As controls, swabs were opened in the room in which the patient cultures were taken and were then put in coded vials. These and the other coded specimens were collected in basal minimal media, inoculated into tube cultures of human embryonic kidney, and examined daily for evidence of viral cytopathic effect.

Those cultures showing cytopathic effect within 7 days were passed to new tube cultures of human embryonic kidney. All cultures that showed evidence of viral growth in the second passage were proved to be those of herpesvirus by neutralization with antisera to herpesvirus. In addition, in a random selection of positive samples herpesvirus type 2 was demonstrated by indirect immunofluorescence.

The compiled data revealed that, of the 190 men studied, 15 percent were positive for herpesvirus. There was no significant difference between age groups

Table 2. Distribution of herpesvirus-positive cultures in genitourinary specimens. The difference between urethral swabs and all other specimens was found to be statistically significant as determined by paired comparisons ($.02 < P < .05$).

Source	Positive cultures (No.)	Men (No.)	Positive for type of sample (%)
Urethral swabs	11	144	7.6
Prostate fluid	3	13	23.1
Prostate biopsy	4	20	20
Vas deferens	9	31	29
Other samples	4	21	19

in the number of positive cultures (Table 1). When these data were analyzed with regard to sample type, however, differences were seen—prostate and vas deferens samples had a higher percentage of positives than did urethral swabs (Table 2). All control swabs were negative. It should be noted that the higher isolation rates found in this study, as compared with rates given in a previous report (7), could have been caused by dissimilar methods of collecting samples.

It is interesting that herpesvirus was isolated from patients with diagnosed cancer. Of the 20 cancer patients (ages 45 to 70), four positive cultures were obtained from urethral swabs, which is a much higher incidence than in the total positive cultures found in urethral swab specimens.

Although well-controlled epidemiologic studies are required, this investigation indicates that the male genitourinary tract, unlike the female genital tract, serves as a reservoir for herpesvirus. The relatively high incidence of positive cultures found in specimens obtained from deeper tissue, such as prostate gland and vas deferens, is consistent with reports of herpesvirus in glandular tissue, such as the lacrimal gland of patients with recurrent herpes keratitis (8).

Since herpesvirus can persist in the

male genitourinary tract in the absence of overt disease, it provides a reservoir for the venereal transmission of the virus and indicates that the relationship of this virus to prostatic cancer or other male genitourinary disease deserves further study.

YSOLINA M. CENTIFANTO

DAVID M. DRYLIE

STEPHEN L. DEARDOURFF

HERBERT E. KAUFMAN

Departments of Ophthalmology and Urology, College of Medicine, University of Florida, Gainesville 32601

References and Notes

1. D. C. Westfield, *Brit. J. Vener. Dis.* **42**, 263 (1966); J. D. J. Parker and J. E. Banatyal, *ibid.* **43**, 212 (1967); A. J. Nahmias, W. R. Dowdle, Z. M. Naib, W. E. Posey, C. F. Luce, *Pediatrics* **42**, 659 (1968).
2. W. E. Rawls, W. A. F. Tompkins, J. Melnick, *Amer. J. Epidemiol.* **89**, 547 (1969).
3. A. J. Nahmias, W. E. Josey, Z. M. Naib, C. F. Luce, A. Duffey, *ibid.* **91**, 539 (1970); I. Royston and L. Aurelian, *ibid.*, p. 531; H. J. Davis, *J. Reprod. Med.* **4**, 109 (1970); E. Adam, A. H. Levy, W. E. Rawls, J. L. Melnick, *J. Nat. Cancer Inst.* **47**, 941 (1971).
4. L. Aurelian, J. D. Strandberg, L. V. Melendez, L. A. Johnson, *Science* **174**, 704 (1971).
5. R. Duff and F. Rapp, *J. Virol.* **8**, 469 (1971).
6. Y. M. Centifanto, R. J. Hildebrandt, B. Held, H. E. Kaufman, *Amer. J. Obstet. Gynecol.* **110**, 690 (1971).
7. S. Jeansson and L. Molin, *Lancet* **1970-I**, 1064 (1970).
8. H. E. Kaufman, D. C. Brown, E. D. Ellison, *Amer. J. Ophthalmol.* **65**, 32 (1968).
9. Supported in part by NIH grants EY00446 and EY00007 and grant CI 21 of the American Cancer Society. The cooperation of Dr. George H. Miller, chief of staff, Veterans Hospital, and professor of urology, is acknowledged.

15 May 1972; revised 8 August 1972

Adaptation of the Adrenal Medulla: Sustained Increase in Choline Acetyltransferase by Psychosocial Stimulation

Abstract. Sustained increases were produced in adrenal choline acetyltransferase of individually caged mice by placing them into groups for 10 or 15 minutes daily for 7 to 10 days. They were left undisturbed in their individual cages for the remainder of each day. As in previous experiments of similar design, adrenal catecholamines and adrenal weight were also increased, although body weight was not affected.

Emotional arousal enhances the release of catecholamines from the adrenal medulla (1). Even short daily periods of intense neural stimulation cause sustained adaptive changes in the chromaffin tissue of the adrenal medulla (2, 3). Activities of adrenal enzymes for catecholamine biosynthesis are increased by neural stimulation only if the preganglionic innervation of the adrenal gland is intact (4). However, the activity of tyrosine hydroxylase, the rate-limiting enzyme for the biosynthesis of the catecholamines, is increased even in denervated adrenal glands by repeated injections of acetylcholine (5). Further,

methedrine, injected into rats for two or more consecutive days, stimulates the release of adrenal catecholamines, and increases the activity of choline acetyltransferase as well as that of tyrosine hydroxylase (6). Fighting depletes catecholamines from the adrenal medulla (7), but repeated fighting causes adaptive increases in adrenal catecholamines (2) and in the enzymes for their biosynthesis (8). From these observations, we reasoned that brief periods of daily fighting should increase the activity of choline acetyltransferase in the adrenal glands of mice.

Male mice were received from the

supplier at 4 weeks of age and were divided into two groups. Mice for experiment 1 were immediately caged individually for 4 weeks to make them aggressive (9). During the last 10 days of this period, three to eight test animals were placed together for 10 to 15 minutes each afternoon to permit them to fight. They were killed by decapitation 18 hours after the last session. Mice for experiment 2 were kept in groups of six until 3 months of age, at which time they were individually housed for 1 month. Test animals were placed in groups for 10 to 15 minutes on each of the last 7 days of this period and were killed by decapitation 18 hours after the last session. Both adrenals from each animal were assayed for choline acetyltransferase and cholinesterase or for epinephrine and norepinephrine. Whole brains (experiment 1) were assayed for choline acetyltransferase and cholinesterase (10).

Mice caged individually for 1 month immediately after weaning (experiment 1) fought intensely when initially placed in groups. However, as in previous experiments (2), the intensity and frequency of fighting declined progressively with repeated exposures to the group situation; during the last three of the ten daily sessions they fought little or not at all. Mice that lived in groups for 2 months before being caged individually for 4 weeks (experiment 2) demonstrated increased motor and exploratory activity during the short periods of daily grouping; but even initially they made only weak, sporadic attempts to fight, and fighting was not observed at all during the last five of the seven daily periods of grouping.

Both total choline acetyltransferase activity of the paired adrenals and enzyme activity relative to protein were greater in the socially stimulated mice than in controls in both experiments (Table 1). The differences in control choline acetyltransferase activity in the two experiments were due to the differences in assay conditions (10). Adrenal cholinesterase activity was not changed by social stimulation (11). As in earlier experiments of similar design (2) adrenal catecholamines and adrenal weight were significantly greater in the stimulated mice than in controls, although body weight was not different (12). Neither choline acetyltransferase activity nor cholinesterase activity was greater in brains of stimulated mice as compared to controls (13). The latter results complement those of Consolo and Valzelli (14), who reported no difference