in CSF originates from oxidative deamination of tryptamine in the brain or from the systemic circulation. There are indications that tryptamine, but not 5-HT or 5-HIAA, enters the brain from the bloodstream (*10*). Lovenberg *et al.* (*11*) have shown that brain contains the enzymes responsible for the transformations tryptophan → tryptamine → IAA. However, it cannot be excluded that IAA also is formed by transamination of tryptophan with subsequent oxidative decarboxylation (*12*). The intermediate in this pathway is indole-3-pyruvic acid.

LEIF BERTILSSON
Departments of Pharmacology (Division of Clinical Pharmacology), Toxicology (Swedish Medical Research Council), and Psychiatry (at Karolinska Hospital), Karolinska Institutet, S-104 01 Stockholm 60, Sweden
LENA PALMÉR
Department of Toxicology, Swedish Medical Research Council, Karolinska Institutet

References and Notes

1. G. W. Ashcroft and D. F. Sharman, *Nature* **186**, 1050 (1960); S. J. Dencker, U. Malm, B.-E. Roos, B. Werdinius, *J. Neurochem.* **13**, 1545 (1966); H. M. van Praag and J. Korf, *Psychopharmacologia* **19**, 148 (1971).
2. A. T. B. Moir, G. W. Ashcroft, T. B. B. Crawford, D. Eccleston, H. C. Guldberg, *Brain* **93**, 357 (1970).
3. G. Curzon and P. K. Bridges, *J. Neurol. Neurosurg. Psychiat.* **33**, 698 (1970).
4. G. Curzon, *Brit. J. Psychiat.* **115**, 1367 (1969).
5. A. Coppen, D. M. Shaw, A. Malleson, E. Eccleston, G. Gundy, *ibid.* **111**, 993 (1965).
6. J. M. Saavedra and J. Axelrod, *Science* **175**, 1365 (1972).
7. W. Lovenberg, E. Jéquier, A. Sjoerdsma, *Advan. Pharmacol.* **6A**, 21 (1968).
8. L. Bertilsson, A. J. Atkinson, Jr., J. R. Althaus, Å. Härfast, J.-E. Lindgren, B. Holmstedt, *Anal. Chem.*, in press.
9. M. Åsberg, L. Bertilsson, D. Tuck, B. Cronholm, F. Sjoqvist, unpublished results.
10. D. F. Sharman, *Brit. Med. Bull.* **21**, 62 (1965).
11. W. Lovenberg, H. Weissbach, S. Udenfriend, *J. Biol. Chem.* **237**, 89 (1962).
12. H. Weissbach, W. King, A. Sjoerdsma, S. Udenfriend, *ibid.* **234**, 81 (1959).
13. We thank E. Dufva, Å. Härfast, and L. Roswall for technical assistance. Supported by grants from the Tri-Centennial Fund of the Bank of Sweden to B. Holmstedt (68/53) and to B. Cronholm and F. Sjoqvist (68/90); by NIH grants GM 13 978 and MH 12007; by grants from the Wallenberg Foundation, Swedish Medical Research Council (B72-40Y-2375-05); and by funds from Karolinska Institutet.

28 February 1972

Yellow Fever Vaccination, Avian Leukosis Virus, and Cancer Risk in Man

Abstract. *Comparison was made between 2659 veterans who died of cancer, during 1950 to 1954 or 1959 to 1963, and matched controls, based on the frequency of yellow fever immunization during World War II. The vaccine was produced from chick embryos that almost certainly contained avian leukosis-sarcoma viruses. Among the veterans, no relation was found between vaccination and leukemia, lymphoma, or other cancer.*

The use of chick embryos in the production of yellow fever vaccine during World War II suggests the presence of viruses capable of inducing neoplasia in avian species. To determine whether the vaccine could also induce cancer in man, we studied cancer mortality among army veterans of World War II in relation to their immunization against yellow fever during military service.

Leukosis-sarcoma viruses are ubiquitous in the avian species—viruses even having been isolated from "leukosis-free" flocks. The cell type of the neoplasia varies according to the strain of virus, and tumors occur mainly in the blood-forming organs, soft tissues, and kidney (*1*). Experimentally, avian viruses have seldom induced neoplasia in mammals, except for the Rous sarcoma virus which, when injected into various species, has induced spindle-cell sarcoma (*2*).

There is little doubt that most, if not all, of the yellow fever vaccine used during World War II was contaminated with avian viruses, but the extent of the contamination cannot be determined today. Although at that time viruses were known to cause avian leukosis, their presence in chick embryos was unknown. Furthermore, a viral origin of human cancer was considered to be remote. Subsequently, with the immense new understanding of viral oncology, the effects of live vaccines used in the past have come into question.

A third or more of World War II army veterans received yellow fever vaccine, but only about 1 percent had died of cancer 20 years later. Hence, a retrospective design, comparing veterans who died of cancer with living veterans on the basis of yellow fever vaccination, was adopted in preference to a prospective design, that is, one in which cohorts of the vaccinated and the nonvaccinated veterans would be compared as to subsequent cancer mortality. Representative deaths from cancer were obtained by sampling notices of death prepared by the Veterans Administration on virtually all deceased war veterans for the years 1950 to 1954 and 1959 to 1963 (*3*). The underlying cause obtained from the death certificate was used to identify deaths from cancer. Death certificates are 80 to 90 percent accurate as to the fact of cancer and about 60 percent accurate at the three-digit level of diagnostic classification (*4*). For lymphomas, death certificates are quite accurate, but for cancer of the pancreas or lung, much less so. For convenience and simplicity, sampling was restricted to white males born between 1912 and 1928 and with World War II service beginning prior to 1945. Similarly restricted controls were obtained from a "2-percent file" representative of National Service Life Insurance numbers

Table 1. Comparison of men who died of cancer with controls on the basis of previous yellow fever vaccination and by type of cancer. ICD, "International Classification of Disease"; +, vaccinated; −, not vaccinated.

Yellow fever vaccination	Cases		Controls	
	No.	(%)	No.	(%)
All forms of cancer (ICD 140–205)				
+	1221	45.9	1174	44.2
−	1438	54.1	1485	55.8
Lymphoma (ICD 200–203)				
+	147	46.1	139	43.6
−	172	53.9	180	56.4
Leukemia (ICD 204)				
+	84	43.5	81	42.0
−	109	56.5	112	58.0
Other cancer (ICD 140–199, 205)				
+	990	46.1	954	44.4
−	1157	53.9	1193	55.6

Table 2. Comparison of men who died of lymphoma with controls on the basis of previous yellow fever vaccination, by date of entry on active duty and by date of death. +, Vaccinated; −, not vaccinated.

Date entered active duty	Yellow fever vaccination	Cases		Controls	
		No.	(%)	No.	(%)
Lymphoma deaths, 1950–1954 and 1959–1963					
Before July 1942	+	76	72.4	77	74.8
	−	29	27.6	26	25.2
July 1942 or later	+	71	33.2	62	28.7
	−	143	66.8	154	71.3
Lymphoma deaths, 1950–1954					
Total	+	45	48.9	43	46.7
	−	47	51.1	49	53.3
Lymphoma deaths, 1959–1963					
Total	+	102	44.9	96	42.3
	−	125	55.1	131	57.7

and individually matched by year of birth and date of insurance (*5*).

The permanent files of personnel and medical records of World War II army veterans include the immunization register, with signed and dated statements for all vaccinations; for yellow fever vaccination the date is always recorded and the vaccine lot number is given for 65 percent of the vaccinations (*6*). Since army personnel were neither all nor randomly immunized (*7*), information for both cases and controls was also abstracted on a number of other variables that might conceivably influence the risk of subsequent cancer, namely, state of birth, urban-rural classification of residence at induction, prior education, civilian occupation, date of entering service, arm or service to which assigned, blood type, cholera or typhus immunizations, overseas theater of service, religion, and rank at separation.

Cases and controls were first compared according to history of vaccination and the type of cancer classified (see Table 1). There is no suggestion of association between yellow fever vaccination and cancer as classified there. This is true not only for the material as a whole, but also when comparisons were controlled on year of birth and other variables mentioned above. The main comparisons were also done in the matched-pair fashion (*8*), with similarly negative results. We divided the material by date of entry into service not only because the vaccination rate changed abruptly and markedly over the period from 1942 to 1944, but also because the vaccine used until April or May 1942 led to a large epidemic of serum hepatitis (*9*), attributed to the use of human serum in the preparation of the vaccine. Vaccine used after 1 June 1942 was prepared without serum. In Table 2 the observations on lymphoma are divided by the date of entering service so as to reflect the change in vaccine. No significant differences were observed within each time interval. Because of the epidemic, all cancer cases and controls were further compared on the basis of the incidence of hepatitis during service—no significant difference was found. Within the cancer series, prior hepatitis was not selectively associated with liver neoplasia.

Table 2 also shows the results by date of death, the deaths from 1950 to 1954 representing an interval of 5 to 13 years after immunization, the deaths from 1959 to 1963, an interval of 14 to 22 years after. Finally, comparisons such as those in Table 1 were repeated for each major group of sites (buccal cavity and pharynx, gastrointestinal, respiratory, and so forth) without finding any evidence that yellow fever vaccination had influenced the risk of subsequent cancer.

A relation between yellow fever vaccination and cancer mortality would have been missed if the latent period were shorter or longer than the interval covered in this study, that is, less than 5 years or more than 22. The sample consisted of healthy young adult males; other persons, such as nonwhites, women, or children, who might be more susceptible to a specific agent, were not included in the study. The study was, however, fairly powerful in the statistical sense, varying, of course, with the frequency of the specific form of cancer examined. For example, the upper limit of a 95-percent confidence interval on the relative risk of lymphoma (relative to that among the unvaccinated) is 1.63; for leukemia it is 1.74; and for all other forms of cancer, 1.24.

TOMMY D. WATERS
PAUL S. ANDERSON, JR.
School of Public Health, University of Oklahoma Medical Center, Oklahoma City 73104
GILBERT W. BEEBE
National Academy of Sciences–National Research Council, Washington, D.C. 20418
ROBERT W. MILLER
Epidemiology Branch, National Cancer Institute, Bethesda, Maryland 20014

References and Notes

1. B. R. Burmester and H. G. Purchase, in *Comparative Leukemia Research*, R. M. Dutcher, Ed. (Karger, Basel, 1969), p. 83; P. S. Sarma, F. Edwards, R. J. Huebner, H. C. Turner, L. Vernon, *ibid.*, p. 169; R. J. Huebner, personal communication.
2. C. G. Ahlström, *Nat. Cancer Inst. Monogr.* **17**, 299 (1964).
3. G. W. Beebe and A. H. Simon, *Amer. J. Epidemiol.* **89**, 636 (1969). For 1950 to 1954, a 9 percent sample previously used by the Follow-up Agency [see (*10*)], and for 1959 to 1963, a 20 percent sample coded as to cause of death by the Veterans Administration were used.
4. I. M. Moriyama, W. S. Baum, W. M. Haenszel, B. F. Mattison, *Amer. J. Pub. Health Nat. Health* **48**, 1376 (1958); M. A. Heasman and L. Lipworth, *Accuracy of Certification of Cause of Death, Studies on Medical and Population Subjects No. 20* (Her Majesty's Stationery Office, London, 1966); S. Jablon, in *Epidemiological Approaches to the Study of Cancer and Other Chronic Diseases*, W. M. Haenszel, Ed. (Government Printing Office, Washington, D.C., 1966), p. 445.
5. It is estimated that 98 percent of World War II army veterans took out National Service Life Insurance, so that the file of insurance numbers fully represents those who served; in addition, the few cancer deaths lacking such insurance numbers were excluded. Matching on date of insurance resulted in 34 percent having the same month of entry into active service, and 72 percent differing by 3 months or less; the mean difference in date of entry was less than 1 month.
6. G. W. Beebe, in *Oncology, 1970, Being the Proceedings of the Tenth International Cancer Congress*, R. L. Clark, R. W. Cumley, J. E. McCay, M. M. Copeland, Eds. (Year Book Medical, Chicago, 1971), vol. 5, p. 364.
7. A. P. Long, in *Medical Department, United States Army. Preventive Medicine in World War II* (Government Printing Office, Washington, D.C., 1955), vol. 3, p. 271; J. R. Paul and H. T. Gardner, *ibid.*, vol. 5, p. 411 (1960).
8. W. G. Cochran, *Biometrika* **37**, 256 (1950).
9. W. A. Sawyer, K. F. Meyer, M. D. Eaton, J. H. Bauer, P. Putnam, F. F. Schwentker, *Amer. J. Hyg.* **39**, 337 (1944); *ibid.* **40**, 36 (1944).
10. This investigation is part of a program of studies of the Follow-up Agency, Division of Medical Sciences, National Academy of Sciences–National Research Council, carried out in cooperation with the Veterans Administration, Department of Defense, and National Institutes of Health, and was supported by contract No. PH43-64-44, T.O. 23 and 54, with the National Cancer Institute.

23 March 1972

Perceiving Real-World Scenes

Abstract. *When a briefly presented real-world scene was jumbled, the accuracy of identifying a single, cued object was less than that when the scene was coherent. Jumbling remained an effective variable even when the subject knew where to look and what to look for. Thus an object's meaningful context may affect the course of perceptual recognition and not just peripheral scanning or memory.*

In experiments on perceptual recognition, a subject typically sees either a single item surrounded by homogeneous space or an array of unrelated ("random") items. In the real world, such meager perceptual experiences are rare. Outside the laboratory, objects are almost always perceived in some setting or context.

Given conventional stimulus displays, it is not surprising that the results of much perceptual research can generally be reconciled with a class of models that hold that the various items of the display are treated as separate entities; that is, they are initially processed independently in a very short-term sensory store (lasting just fractions of a second), and then transferred serially to a longer-term storage system [see (*1*)]. It is in this longer-term storage system that meaningfulness and long-term