tract appears to be a macromolecule with a mass of approximately 30,000 to 50,000 daltons; it is thermolabile and destroyed by trypsin. It is apparently not stable on long-term storage, even in the cold.

JOHN C. HOUCK, HILTJE IRAUSQUIN
SANFORD LEIKIN
Research Foundation of the Children's Hospital of the District of Columbia, Washington, D.C. 20009, and George Washington University School of Medicine, Washington, D.C. 20005

References and Notes

1. W. Bullough and E. Laurence, *Proc. Roy. Soc. London Ser. B* **151**, 517 (1960); *Exp. Cell Res.* **33**, 176 (1964); *Nature* **220**, 134 (1968).
2. ———, *Eur. J. Cancer* **4**, 607 (1968).
3. J. Rytomaa and K. Kiviniemi, *Cell Tissue Kinet.* **1**, 329 (1968).
4. J. Simnett and D. Chopra, *Nature* **222**, 1189 (1969).
5. M. Voaden, *Exp. Eye Rse.* **7**, 326 (1968).
6. J. Moorhead, E. Paraskova-Tchernozemska, A. Pirrie. S. Hayes, *Nature* **224**, 1207 (1969).
7. E. Zipilivan, B. Hudson, W. Blatt, *Anal. Biochem.* **30**, 91 (1969).
8. Supported in part by a contract from the Medicine and Dentistry Division of the Office of Naval Research.

24 May 1971

Talc-Treated Rice and Japanese Stomach Cancer

Abstract. *The Japanese prefer talc-dusted rice in their diet. The incidence of stomach cancer in Japan is unusually high. Most talc has some asbestos contaminants. Epidemiologic evidence is presented that the asbestos-contaminated talc on rice in the diet is the carcinogen or cocarcinogen responsible for the high incidence of Japanese stomach cancer.*

The high incidence of stomach cancer in Japanese men represents a challenging problem in cancer epidemiology. Study of age-adjusted rates of mortality from stomach cancer in 24 countries showed that from 1962 to 1963 Japanese men had the highest rate for all nations; the rate, 67.96 per 100,000 in the male population, was seven times that for men in the United States (*1*). Since talc frequently contains asbestos (*2*), and since workmen exposed to asbestos show a marked increase in gastrointestinal cancer, especially stomach cancer (*3*), the hypothesis that the increased rate of cancer of the stomach in Japan is due to ingestion of rice contaminated with asbestos seems attractive and has been recently suggested in a brief note (*4*). This report presents evidence for this relationship at somewhat greater length.

Rice grown in California and meant for the American consumer is milled mechanically. Rice is prepared differently for the Japanese consumer. It is milled and treated with glucose, and then talc is added. The talc is held to the surface of the grain and is said to preserve its flavor better. Japanese consider this rice more tasty, both here and in Japan. Two percent of all talc produced in California from 1959 to 1963 was used as a rice additive, primarily for export to Japan (*5*). Rice containers in Los Angeles markets intended for the Japanese customer usually bear the legend: "Coated with glucose and talc." Optical microscopy of the ash of such store-bought rice showed 3.7×10^6 asbestos-form fibers per gram (Fig. 1).

Talc, the mineral, is a hydrous silicate of magnesium. So are some forms of asbestos. The difference between these two minerals is not in their chemical compositions, but rather in their structure, asbestos being fibrous and mineral, talc being flaky or granular. However, commercial talc is composed not only of the pure mineral talc, but also of fibrous silicates, which are in part classifiable as asbestos. There is no firm mineralogic definition of commercial talc, and in most areas the mineral talc forms much less than half of commercial talc. The composition of commercial talc varies with the deposit. Vermont mines produce a platy or granular type of mineral relatively free of asbestos minerals (*6*). New York and California talcs contain more fibrous silicates, including anthophyllite and tremolite (*2, 5*).

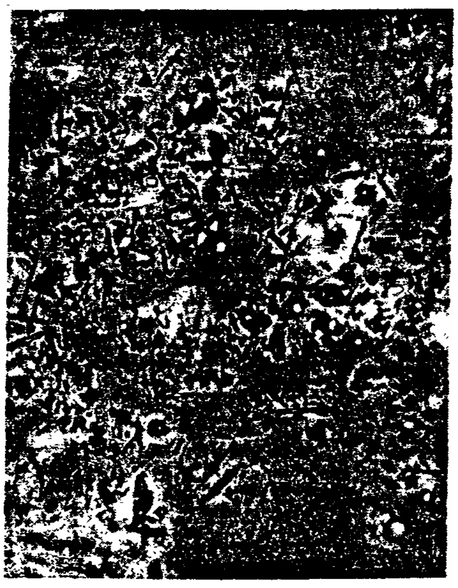

Fig. 1. Photomicrograph of the ash of a specimen of rice intended for Japanese consumption and purchased in a Los Angeles market. Arrows indicate asbestos-form fibers. The specimen contained 3.7×10^6 such fibers per gram.

Respired asbestos and talc dust cause similar disorders in workmen. Older talc workers show more than four times the expected incidence of lung and pleural cancer (*7*). Talc or talcose minerals, including contaminating asbestos, are apparently the responsible carcinogens since, where confirmatory evidence could be obtained, all those talc workers with pleural and lung cancer also had talc pneumoconiosis. Autopsies on six talc workers with talc pneumoconiosis showed the presence of the characteristic "asbestos body" in the lungs of every one (*8*). When talc is examined by phase contrast microscopy, from 8 to 30 percent of the particles are fibrous silicates. Identifiable tremolite, anthophyllite, and chrysotile are also seen (*9*). The large talc deposits of New York and California regularly contain the amphibole asbestos minerals, tremolite and anthophyllite. These are normal ingredients of commercial talcs from these areas. Chrysotile asbestos occurs in veins in talcose mineral deposits and may be then mined with the talc and create a contaminant (*9*).

Asbestos is an established carcinogen. Not only does it cause lung cancer, but it is associated with a substantial increase of morbidity from stomach cancer (*3*). Although chrysotile is the most important commercial fiber of asbestos, there is no reason to regard the amphibole asbestos minerals as safe. To the contrary in one study an amphibole asbestos mineral predominated in asbestos-bodies in the sputum of a group of men exposed to asbestos and having a high incidence of mesotheliomata (*10*). The fact that talc workers exposed to fibrous talc, which contains amphibole asbestos, develop more pulmonary injury than do workers exposed only to talcs relatively free of fibrous silicates or amphiboles (*11*), indicates the pathogenicity of amphibole asbestos.

The Japanese preference for talc-coated rice means that rice eaters of that nation are exposed to the hazard of ingestion of amphibole asbestos, as well as the unpredictable ingestion of chrysotile in areas where talc contains these carcinogenic materials.

Examination of the known epidemiologic characteristics of stomach cancer in Japanese strongly suggests that the causative agent is an additive to rice. Not only is the incidence of stomach cancer high in rice-eating Japanese, but inside Japan stomach cancer is most prevalent in those prefectures where rice is the main staple; it is less so in prefectures where rice is supplemented with cereal (*12*) and where the population eats heavily of the soybean preparations shoyo and miso (*13*). The morbidity from stomach tumors is greater among Japanese who eat rice with every meal than it is among Japanese who eat it less often; among Japanese men who like milk and vegetables there is a lesser morbidity from stomach neoplasms (*14*). Experimental consumption of polished rice will cause ulceropapillomata of the forestomach of rats (*15*).

These observations suggest a relationship between rice consumption and stomach cancer. However, the agent is not the rice itself, since in other oriental countries where talc-coated rice is not popular the incidence of stomach cancer is not unduly high.

A final indication of the environmental causes of stomach cancer in Japanese is provided by statistics concerning its prevalence in Japanese immigrants to western countries. The incidence in Japanese males in Japan in 1962 to 1964 was 77.9 per 100,000 (*16*). Japanese men in Hawaii had an incidence of only 45 per 100,000. Even this lowered rate was high compared to that for Chinese and Caucasian men of Hawaii who had incidences of 9.2 and 8.3, respectively. Native-born Japanese have a higher incidence of stomach cancer than Japanese born in Hawaii or continental North America (*17*). Dietetic studies on immigrant Japanese show that from 50 to 70 percent of their diet is Japanese-type food (*18*). The longer the immigrant has been in the West the more western his diet becomes; this increase in western food in the diet coincides with a decrease in the incidence of stomach cancer.

The hypothesis that the carcinogenic agent causing the high incidence of Japanese stomach cancer is asbestos-containing talc on rice appears therefore to satisfy the characteristics of the known epidemiology of that form of cancer in Japan. However, standardized mortality rates are also high for Chile, Finland, and Iceland, where rice is not a major dietary staple (*12, 19*). In view of the evidence for the Japanese, the presence of asbestos-contaminated talc as an additive to some nationally popular food should be suspected in these countries. Further studies of the total contamination of the common diet by talc and asbestos in these nations with high incidences of stomach cancer are needed.

R. R. MERLISS

8820 Wilshire Boulevard,
Beverly Hills, California 90211

References and Notes

1. T. Hirohata and M. Kuratsume, *Br. J. Cancer*, 23, 465 (1969).
2. L. A. Wright, *Talc and Soapstone* (California Division of Mines Publications, Bulletin 176, San Francisco, 1957).
3. I. Selikoff, J. Churg, E. Hammond, *J. Am. Med. Assoc.* 188, 22 (1964).
4. R. Merliss, *ibid.* 216, 2144 (1971).
5. J. R. Wells, in *Mineral Facts and Problems* (U.S. Bureau of Mines, Washington, D.C., 1965).
6. B. Weiss and E. Boehner, *Arch. Environ. Health* 14, 304 (1967).
7. M. Kleinfeld, J. Messite, O. Kooyman, M. Zaki, *ibid.*, p. 663.
8. M. Kleinfeld, C. Giel, J. Majeranowski, J. Messite, *ibid.* 7, 101 (1963).
9. L. Cralley, M. Key, D. Groth, W. Lainhart, R. Ligo, *Am. Ind. Hyg. Assoc. J.* 29, 35 (1968).
10. J. Stumphuis and P. Meyer, *Ann. Occup. Hy* 11, 283 (1968).
11. J. Messite, G. Reddin, M. Kleinfeld, *Am. Med. Assoc. Arch. Ind. Health* 20, 408 (1959
12. M. Segi and M. Kurihara, *Tohuku J. Ex Med.* 72, 169 (1960).
13. M. Segi, L. Fukushima, S. Fujisaku, M Kurihara, S. Saito, K. Asano, M. Kamo *Gann* 48 (Suppl.), 1063 (1957).
14. I. Hirayama, in *Proceedings of the International Conference on Gastric Cancer* (Maruzen, Tokyo, 1968).
15. A. Braunschwig and R. A. Rasmussen, *Cancer Res.* 1, 371 (1941).
16. R. Doll, P. Payne, J. Waterhouse, *Cancer Incidence in Five Continents* (Springer-Verlag, New York, 1966).
17. W. B. Quisenberry, *Acta Unio Int. Contra Cancrum* 17, 858 (1961).
18. W. MacDonald, *Canadian Cancer Conference 6th* (1966), pp. 451–459.
19. N. Dungal and J. Sigurjonsson, *Br. J. Cancer* 21, 270 (1967).

7 June 1971

Cyclic Adenosine Monophosphate in Brain Areas: Microwave Irradiation as a Means of Tissue Fixation

Abstract. *Amounts of cyclic adenosine monophosphate in discrete regions of the brain were estimated after exposure of rats to microwave irradiation. Amounts were highest in the cerebellum and brainstem, intermediate in the hypothalamus and midbrain, and lowest in the hippocampus and cortex. Decapitation increased the concentration of cyclic adenosine monophosphate in all brain areas, although the increase in the cerebellum was three to four times greater than that in other areas. Microwave irradiation may provide a means of rapidly fixing brain tissue in situ while permitting easy dissection of the brain. In this way artifacts produced by decapitation can be eliminated, and concentrations of heat-stable compounds in the brain can be estimated under conditions which more closely approximate those in vivo.*

Rapid fixation of cerebral tissue in situ is required to obtain valid estimates of many brain components. Decapitation and delayed fixation lead to significant changes in brain glycogen (*1*) and in glucose, lactic acid (*2*), and other substrates and cofactors of the Embden-Meyerhof pathway (*3*). At present fixation of the brain in situ is carried out by freezing whole animals in liquid nitrogen or cooled isopentane. Even under such conditions, deep brain structures can require up to 75 seconds to reac 0°C (*4*). These freezing techniques al require restraint of the animal and pr duce considerable stress before it di Dissection of the frozen brain is alm impossible, and therefore experimen must be done on whole brains. Th problems have prevented the measu ment of cyclic adenosine monoph phate (AMP) in discrete brain regio Drug-induced changes in concentratio of cyclic AMP in specific brain ar might easily be masked by mass amounts of unresponding tissue wh nucleotide concentrations are measur in the frozen whole brain. Furthermo the concentration of cyclic AMP in t whole brain increases severalfold wi in seconds after decapitation there prohibiting rapid dissection after de (*5*). Stavinoha (*6*) reported that amou of acetylcholine in the brains of r that had been killed by being expo to microwave irradiation were sig cantly higher than previously repor

Table 1. Amounts of cyclic AMP in brain areas after microwave irradiation. Values represent the mean and standard error of the mean from six separate determinations.

Area	Cyclic AMP (nmole/g)
Cerebellum	1.86 ± 0.06
Brainstem	1.87 ± 0.06
Hypothalamus	1.60 ± 0.04
Midbrain	1.43 ± 0.11
Hippocampus	0.84 ± 0.09
Cortex	0.74 ± 0.06

Vol. 173