[4] Schofield, J. G., *Nature*, **215**, 382 (1967).
[5] Schofield, J. G., *Biochem. J.*, **103**, 331 (1967).
[6] Krebs, H. A., and Henseleit, A., *Z. Physiol Chem.*, **210**, 33 (1932).
[7] Bressler, R., Vargas-Cordon, M., and Lebovitz, M. D., *Diabetes*, **17**, 617 (1968).
[8] Peng, T. C., *Endocrinology*, **86**, 202 (1970).
[9] Miele, E., in *Prostaglandins, Peptides and Amines* (edit. by Mantegassa, P., and Horton, E. W.), 83 (Academic Press, 1969).
[10] Kayaalp, S. O., and Turker, R. K., *Europ. J. Pharmacol.*, **3**, 139 (1968).
[11] Coceani, F., Dreifuss, J. J., Puglisi, L., and Wolfe, L. S., in *Prostaglandins, Peptides and Amines* (edit. by Mantegassa, P., and Horton, E. W.) (Academic Press, 1969).
[12] Curri, S., and Paoletti, R., *Boll. Soc. Ital. Biol. Sper.*, **32**, 1415 (1956).

Effects of High Levels of Yeast Feeding on Uric Acid Metabolism of Young Men

THE possible use of single cells of yeast and bacteria as food is receiving much attention[1,2]. It has long been recognized[3–9] that feeding yeast can increase urinary uric acid excretion, but the levels of its use in processed foods have been so low that no problems have arisen. If yeast and other single cells are used, however, as sources of protein rather than of vitamins, the intakes involved are much higher.

Man and higher apes lack the enzyme uricase, which catalyses the oxidation of uric acid to the more soluble allantoin, so that in individuals with a genetic tendency to primary over-production of uric acid there may be precipitation of uric acid crystals in joints (gout), soft tissues (tophi) or the formation of stones in the urinary tract. The increase in uric acid secondary to a high intake of dietary purines and other exogenous factors may have a similar effect.

Four healthy male MIT students aged 18 to 27 years, weighing 65 to 90 kg, were fed a controlled, low-purine diet providing adequate calories, minerals, and vitamins together with 100 g of protein and about 11 mg purine nitrogen per day. The subjects received the basal diet for 16 days followed by consecutive 9-day periods with 45, 90, and 135 g of food yeast (*Torula utilis*, NF 12 Type 300, Lake States Division, St Regis Paper Co.) distributed equally among four meals. Total protein intake was maintained at 100 g per day. The weight of the subjects remained constant throughout the experiment.

The experimental diets contributed 2·9, 5·8 and 8·7 g of yeast nucleic acid (DNA and RNA) by analysis[10]. Uric acid was determined[11] on plasma taken at 8.00 h, 11 h after the start of the last meal. Creatinine excretion[12] was measured daily throughout the experiment.

The results in Table 1 show that 45 g of yeast containing 2·9 g of nucleic acid was sufficient to raise the serum uric acid levels of the subjects to approximately 7·0 mg/100 ml. Doubling this quantity increased the uric acid levels of all subjects to unacceptable levels, and tripling it brought about a further but much smaller increase.

The only comparable data are those of Waslien *et al.*[13], who fed healthy young men 0, 2, 4 and 8 g of yeast RNA for 5 consecutive days in a constant 75 g egg-protein diet distributed among four equal meals. The resulting average uric acid levels of 4·9, 6·0, 7·7 and 9·4 mg/100 ml. are similar to ours when allowance is made for differences in the exact level of nucleic acid fed. All five of their subjects fed 2 g of yeast RNA had serum uric acid levels which remained within normal limits, while all four of our subjects fed 2·9 g of nucleic acid had levels which were at or slightly above 7·0 mg/100 ml.

Because this is a level which separates most patients with primary gout from most normal subjects[14–16], the combined results for blood uric acid levels suggest that 2 g of single-cell protein (SCP) nucleic acid per day is probably a safe limit to feed most normal subjects, but 3 g of SCP nucleic acid per day might place some normal subjects at risk.

The influence on urinary uric acid excretion of feeding the yeast is shown in Table 1. The lowest level of yeast nucleic acid fed, 2·9 g, increased uric acid excretion to more than 1,000 mg per day, and the additional increase was proportional when nucleic acid ingestion was doubled. A further increase in nucleic acid intake did not produce any consistent further change.

The urinary uric acid excretion values reported by Waslien *et al.*[13] were lower—373, 667, 939 and 1,393 mg per day for the intakes cited previously—but our data suggest that for most normal individuals a daily intake of approximately 3 g of SCP nucleic acid results in undesirably high levels of urinary uric acid because the majority of normal persons on ordinary diets excrete less than 600 mg of uric acid per day[17,18]. A dietary level of 2 g of SCP nucleic acid would seem to involve little risk of stone formation; slightly higher levels probably pose no hazards as long as urine volume and *p*H are not abnormally low. At no time was any gastrointestinal disturbance encountered even at the level of 135 g of yeast per day.

Table 1. EFFECT OF YEAST NUCLEIC ACID ON SERUM AND URINARY URIC ACID IN YOUNG MEN

	Serum uric acid (mg/100 ml.)				Urine uric acid (mg/24 h)			
Yeast fed (g/day)	0*	45	90	135	0*	45	90	135
Yeast nucleic acid intake (g/day)	—	2·9	5·8	8·7	—	2·9	5·8	8·7
Subject number								
1	4·5	7·5	9·2	10·1	533	1343	2007	2100
2	4·7	7·4	9·1	9·9	405	1200	1880	2400
3	4·5	6·8	8·6	8·5	504	1100	1800	1585
4	4·3	7·2	8·5	9·1	599	1125	1725	1400

* 100 g "purine-free" protein per day.
The values for serum and urine uric acid are the means of the values for the 5th, 6th and 7th days of each dietary period.

This work was supported by the John A. Hartford Foundation.

J. C. EDOZIEN
U. U. UDO
V. R. YOUNG
N. S. SCRIMSHAW

Department of Nutrition and Food Science,
Massachusetts Institute of Technology,
Cambridge, Massachusetts 02139.

Received December 15, 1969; revised March 3, 1970.

[1] Mateles, R. I., and Tannenbaum, S. R. (eds.), *Single-Cell Protein* (MIT Press, Cambridge, Massachusetts, and London, 1968).
[2] *International Action to Avert the Impending Protein Crisis* (United Nations, New York, 1968).
[3] Wintz, H., *Munch. Med. Wschr.*, **63**, 445 (1916).
[4] Salomon, H., *Munch. Med. Wschr.*, **63**, 454 (1916).
[5] Funk, C., Lyle, W. G., and McCaskey, D., *J. Biol. Chem.*, **27**, 173 (1916).
[6] Anderson, A. K., *Penn. St. Univ. Agric. Exp. Stat. Bull.*, **367**, 7 (1938).
[7] Dirr, K., *Biochem. Z.*, **312**, 233 (1942).
[8] Murlin, J. R., and Mattill, H. A., *Amer. J. Physiol.*, **64**, 275 (1923).
[9] von Loesecke, H. W., *J. Amer. Dietet. Assoc.*, **22**, 485 (1946).
[10] Maul, S. B., Sinskey, A. J., and Tannenbaum, S. R., *Nature*, **228**, 181 (1970) (this issue).
[11] Liddle, L., Seegmiller, J. E., and Laster, L., *J. Lab. Clin. Med.*, **54**, 903 (1959).
[12] Pino, S., Benotti, J., and Gardyna, H., *Clin. Chem.*, **11**, 664 (1965).
[13] Waslien, C. I., Calloway, D. H., and Margen, S., *Amer. J. Clin. Nutr.*, **21**, 892 (1968).
[14] Gjørup, S., Poulsen, H., and Practorius, E., *Scand. J. Clin. Lab. Invest.*, **7**, 201 (1955).
[15] Grayzel, A. I., Liddle, L., and Seegmiller, J. E., *New Engl. J. Med.*, **265**, 763 (1961).
[16] Gutman, A. B., and Yü, T.-F., *Amer. J. Med.*, **23**, 600 (1957).
[17] Gutman, A. B., and Yü, T.-F., *Amer. J. Med.*, **45**, 756 (1968).
[18] Seegmiller, J. E., Laster, L., and Howell, R. D., *New Engl. J. Med.*, **268**, 712 (1963).