It seems probable that physiological activities of the nucleus on which the cell depends for long-term normal function depend somehow on the conditions existing in the interphase nucleus. It is not difficult to propose reasons why this should be the case. First, it is quite conceivable that the condensed condition of the chromosomes during division is incompatible with their functioning. Perhaps it would be more proper to say that the highly dispersed condition during interphase is more compatible with the essentially two-dimensional "template" functions that are currently the subject of so much interest (*15, 16*). Second, the hypothesis that the specific functions of the chromosomes depend on their being provided with an appropriate intranuclear environment (*17*) would lead one to predict important alterations in chromosomal function during division, when the nuclear membrane is altered or absent. Finally, and on a somewhat different level, the disappearance of the nucleolus during division should be noted. There is now excellent evidence that the nucleolus is an important center of nuclear function (*18*). If this structure, as has been proposed, mediates in the action of the chromosome on the cytoplasm, it is only to be expected that such action will not be observed in the dividing cell where it is absent.

The present experiments obviously do not favor any one of these alternatives or even limit the possibilities to these three. They do, however, tend to prove what has been suspected: that the contributions of the nucleus to cell function depend on the conditions characteristic of its state when it is not dividing and that the condensed thread so useful to the cytologist is a very poor model for a working chromosome.

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Fungitoxicity of Ethylenethiourea Derivatives

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THE ability to predict fungitoxicity of compounds has been, and continues to be, an elusive but much desired goal. Clues to structural changes that appear to increase activity are many. It is only seldom, however, that a suggested change, based on rationale, results in the creation of a fungitoxic molecule from a configuration that is completely inactive. This is a report of one such case (*1*).

The inactive compound chosen for modification was ethylenethiourea. This heterocylic nitrogen compound is similar in structure to the imidazolines and pyrazoles, derivatives of which have been found to be very fungitoxic (*2, 3*). In addition, ethylenethiourea contains a thioketone group that is present in many fungicides, particularly the derivatives of dithiocarbamic acid. Ethylenethiourea, therefore, appears to have many of the requirements of a fungitoxic compound; yet, it is inactive when tested for fungitoxicity by the depression slide technique (*4*).

A second reason for interest in ethylenethiourea is that it has been identified (*5*) as one of the break-down products of nabam (disodium ethylenebisdithiocarbamate). Because of its lack of fungitoxicity, it was thought, however, that this compound could not be directly involved in the fungitoxicity of nabam. Could it be, however, that ethylenethiourea is unable to penetrate through the semipermeable membrane of the spore to the site of action? It is possible that nabam, or one of its intermediate break-down products, penetrates readily, decomposing inside to release ethylenethiourea *in situ*. If this were so, then ethylenethiourea itself could exert fungitoxicity if it were changed in such a way as to increase penetration to the site of action within the spore.

One of the simpler methods of increasing penetration is the addition of a hydrocarbon substituent to the molecule (*6*). This possibility was examined by measuring the fungitoxicity of some alkyl-substituted derivatives of ethylenethiourea (*7*). These were propylenethiourea, N,N′-di-n-butylethylenethiourea, N-n-octylethylenethiourea, N-t-octylethylenethiourea,

Table 1. Fungitoxicity data for ethylenethiourea and certain of its homologs. Data given as percentage inhibition of spore germination at various dosages (μ/cm^2).

Compound	*S. sarcinaeforme*				*M. fructicola*			
	1300	130	13	1.3	1300	130	13	1.3
Ethylenethiourea	0	0	0	0	0	0	0	0
Propylenethiourea	92	0	0	0	100	17	0	0
N,N′-di-n-butylethylenethiourea	54	0	0	0	100	100	5	0
N-n-octylethylenethiourea	100	100	0	0	100	100	100	0
N-t-octylethylenethiourea	0	0	0	0	0	0	0	0
N-n-octadecylethylenethiourea	100	57	0	0	100	100	0	0

and N-n-octadecylethylenethiourea. Fungitoxicity to spores of *Stemphylium sarcinaeforme* (Cav.) Wilts. and *Monilinia fructicola* (Wint.) Honey was determined by using the depression-slide dilution technique.

The data are given in Table 1. Against *S. sarcinaeforme,* propylenethiourea and the N,N′-di-n-butyl derivative were weakly toxic. N-n-octylethylenethiourea was the most toxic of the series (*8*). The N-n-octadecyl derivative was less toxic than the N-n-octyl derivative, while N-t-octylethylenethiourea was completely nontoxic. The derivatives fungitoxic to *S. sarcinaeforme* were even more active against *M. fructicola.* The order of toxicity to *M. fructicola,* however, was about the same as for *S. sarcinaeforme.* The only change in rank was in the case of N,N′-di-n-butylethylenethiourea, which was very weakly fungitoxic to *S. sarcinaeforme* but was second most active against *M. fructicola.*

Concerning the fungitoxicity of these compounds, certain points are apparent. Ethylenethiourea can be made into a fungitoxic compound by the addition of an alkyl side chain. As in the case of imidazoline homologs (*2*), fungitoxicity increases with the length of the carbon chain to a certain point and then diminishes as the chain becomes longer. The side chain must be normal to achieve its effect, as was previously found (*9*) for the fungitoxicity of a series of thiophene derivatives. The fungitoxic derivatives are distinctly more active against *M. fructicola* than they are against *S. sarcinaeforme,* which is what Horsfall found for the action of compounds with lipophilic substituents on these fungi (*10*). Miller, McCallan, and Weed (*11*) showed that spores of *M. fructicola* accumulate more (1380 ppm) at a single dosage of a lipophilic material (2-heptadecyl-2-imidazoline) than do the spores of *S. sarcinaeforme* (860 ppm).

From these data, can it be dedueed that ethylenethiourea may be directly involved in the fungitoxicity of nabam? Two points argue against it. First, the homologs of ethylenethiourea are definitely more toxic to *M. fructicola* than they are to *S. sacinaeforme,* the reverse of nabam (*12*). Second, the toxicity of these compounds does not approach that of nabam. These differences may arise from the fact that nabam is a water-soluble compound that ionizes and hydrolyzes readily. Hence, its ability to permeate into spores would be quite different from that of the fungitoxic derivatives of ethylenethiourea. The apparent discrepancies certainly do not negate the evidence that ethylenethiourea does indeed possess inherent fungitoxicity. This being so, it is entirely possible that ethylenethiourea released *in situ* may be involved directly in the fungitoxicity of nabam.

It is significant that so many different clues have been found to explain the fungitoxicity of nabam (*5, 13–15*). This points to the possibility that nabam may owe its effectiveness to its versatility as a poison or as a source of poisons. If nabam, or its subsequent break-down products, is able to inhibit or destroy many different life-processes, it is much more likely to block alternative vital mechanisms. This would allow fungi and their spores fewer chances for survival.

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