intumescence (39 μ) was exhibited on a tube not exceeding 144 μ. Although not as extreme, similar observations were by no means exceptional. It may further be mentioned that, although not oncogenic, the weaker concentrations of chloroform had a tendency to depress the average length of the pollen tubes. As opposed to the effects of colchicine *a* and *b* on tumor growth vs. elongation, those of chloroform were in consequence far from being consistent.

As can be seen, 2% colchicine *b* prevented germination altogether. In the other concentrations the percentage of germination of the pollen grains was in fair agreement with the length attained by the pollen tubes and in inverse relation to the oncogenic potency and the toxicity of the various concentrations of the drugs. Chloroform at 0.125% was once more an exception to this rule. Some of the very considerable divergency in the rate of germination at the very beginning of the experiment may be ascribed to the chance distribution of the large (46 μ–54 μ) and small (30 μ–35 μ) pollen grains, for, as was empirically demonstrated, the former germinated much earlier than the latter. However, such sources of error were, as can be seen, automatically eliminated by the end of each experiment when maximum growth was attained.

Although in most plants the threshold of the oncogenic influence of colchicine upon roots is higher than the threshold value of its stathmokinetic action, the pollen tubes of *Colchicum* were found to be 10–25 times more sensitive to the oncogenic effects of the drug than were the roots to its stathmokinetic activity, according to the findings of Cornman. Yet, when compared with the reactivity of other plants—e.g., wheat, in which germination and growth are completely stopped at 0.4% and tumors are found at 0.0075%—even the pollen tubes of *Colchicum* were found to display a marked resistance to the alkaloid.

In view of the practically identical oncogenic action of colchicine plus chloroform of crystallization and colchicine from which the chloroform was removed, previous axiomatic assertions (*2, 3*), including that of the senior author (*1*), regarding the total immunity of the plant to the alkaloid can hardly be maintained. The findings of Cornman are thus complemented and implicitly confirmed.

Production of pollen tube tumors in *Colchicum* confirms the oncogenic action of chloroform reported by Steinegger and Levan (*7*) for *Allium*. Our experiments do not, however, substantiate a generalization of the thesis of Levan and Steinegger, according to which the action of the alkaloid in *Colchicum* is to be ascribed to the chloroform of crystallization in the drug. In fact, the above-mentioned inversion of the logically inferable respective growth effects and oncogenic potency of 0.05% vs. 0.1% chloroform, as well as the remarkable difference in the length of tubes with colchicine- vs. chloroform-induced swellings, seem to justify the hypothesis, suggested by Cornman, that different mechanisms are operating.

It is readily admitted that, as they now stand, our investigations emphasize rather than resolve the enigmas associated with the complex problem of immunity. Nevertheless, it is hoped that by confirming, in refractory material such as *Colchicum*, the existence of different oncogenic sensitivities and reactivities in different organs of the same organism, search for their active principle will be encouraged. Given the chemotherapeutic implications of the oncogenic (*1, 8, 9*) and oncolytic (*10, 11*) actions of colchicine in both plants *and* animals, it may not be too far-fetched to recall that also among the animals many were thought resistant to various carcinogens, including colchicine, until the appropriate site of administration had been discovered.

Addendum: According to a personal communication from Dr. Cornman, received when this article was ready for press, the colchicine used by him contained no chloroform. The susceptibility of *Colchicum* to colchicine is thus mutually confirmed.

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Changes in Biliary Cholesterol in Abnormal Thyroid States[1, 2]

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It has long been realized that an inverse relationship exists between plasma cholesterol concentration and the level of thyroid activity (*1*). In general, hyperthyroidism is associated with a decreased plasma cholesterol level and hypothyroidism with an elevated concentration, although these changes are not always striking (*2*). The mechanism underlying this relationship remains unexplained. Recent studies from this laboratory (*3–5*) suggested to us the possibility that knowledge of the bile cholesterol content in abnormal thyroid states might help to clarify this important problem.

Two separate series of male Long-Evans rats, aged 8 and 13 weeks, respectively, were studied. Each series consisted of three groups. One group (control) of the first series was fed a stock diet for 28 days; the sec-

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TABLE 1

Type of rat	No. of rats	Average wt		Daily vol of bile (ml)	Bile cholesterol	
		Initial (g)	Final (g)		Concentration (mg/100 ml)	Daily output (mg)
			Series 1			
Control	6	—	181	11.1	27 (22–36)*	2.9 (1.9 – 3.8)
Hypothyroid	6	174	190	9.8	13 (12–14)	1.2 (1.1 – 1.3)
Hyperthyroid	10	150	158	10.0	45 (27–62)	4.4 (2.7 – 6.2)
			Series 2			
Control	10	249	310	14.5	17 (13–20)	2.4 (1.7 – 3.4)
Hypothyroid	11	232	266	13.2	8 (4–13)	1.1 (0.35– 2.0)
Hyperthyroid	7	252	308	19.4	38 (21–61)	7.4 (3.9 –11.5)

* Figures in parentheses represent range.

ond group of the same series was given stock diet plus powdered thiouracil (constituting 0.25% of the diet) for 33 days, and the third group received stock diet plus powdered thyroid substance (constituting 0.12% of the diet) for 18 days. The second series was maintained for 42 days, controls receiving stock diet, the second group receiving thiouracil in addition as 0.3% of the diet, and those given thyroid substance receiving this material as 0.3% of the diet. Dietary supplements administered as above have been shown (*6*) to induce hypothyroidism and hyperthyroidism, respectively, in rats. The general condition, weight changes, and behavior of our groups of rats confirmed this observation.

At the termination of the feeding periods, the bile duct of each rat was catheterized (*3*), and bile was collected for 24 hr. Bile cholesterol was extracted from each individual 24-hr sample according to the method of Foldes (*7*) and analyzed according to an adaptation of the method of Saifer and Kammerer (*8*), as described previously (*3–5*).

As Table 1 demonstrates, the hyperthyroid rat in both series was found to excrete far more cholesterol in his bile than the normal animal. Thus, in the first series, both the concentration of cholesterol in the bile and the daily biliary excretion of cholesterol were almost twice that found in the control rat. In the second series, more than twice the control amount of biliary cholesterol was excreted by the hyperthyroid rat. Conversely, the biliary concentration and daily output of cholesterol in the hypothyroid rat was about half that found in the normal control rat. It should be mentioned that the variations observed between the first and second series were quantitative, not qualitative, and very possibly were attributable to differences in age and weight of the animals in the two series (*9*).

This disturbance in biliary concentration and output of cholesterol in thyroid derangement represents a second abnormality in the metabolism of this steroid in thyroid dysfunction. The previously known abnormality—namely, the alteration in plasma concentration of cholesterol—is a change, the opposite in direction to the present biliary findings. The mechanism responsible for both the biliary and the plasma changes of cholesterol concentration in thyroid derangement is now under investigation.

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Notes on the Strontium Content of Sea Water, Celestite Radiolaria, and Strontianite Snail Shells[1]

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I. The strontium value of sea water has been in doubt because of the wide range in reported values. The values of strontium in mg/l for a salinity of 35 parts/mille as reported by different workers with different methods are as follows: Desgrez and Meunier (*1*), 8.7; Thomas and Thompson (*2*), 13.2; Ramage (*3*), 40.–50.; Noll (*4*), 7.0–7.9; Miyake (*5*), 14.4; Vinogradov (*6*), 8.0; and Vinogradov (*7*), 10.0.

In the present study 235 determinations of Sr/Ca ratio have been made on 160 samples from diverse parts of the Atlantic, including samples in all seasons from Long Island Sound, deep samples from the middle Atlantic and opposite Gibraltar, and samples from the Gulf Stream.[2] Arc and flame spectrophotometric methods were used on single and double oxalate precipitations. The preferred value of atomic Sr/Ca ratio from these analyses is 9.23 atoms/1,000 atoms

[1] From a dissertation on The Biogeochemistry of Strontium, presented to the faculty of Yale University in partial fulfillment of requirements for the Ph.D. degree. The stimulating direction of G. E. Hutchinson is gratefully acknowledged.

[2] Collected by Bingham Oceanographic Laboratory and Woods Hole Oceanographic Laboratory and made available by G. A. Riley, E. F. Thompson, and Dean Bumpus.