whether pyrexin can be in large part inactivated, while leaving behind an active leukopenic factor. The scheme of extraction adopted follows:

SCHEME OF EXTRACTION OF LEUKOPENIC FACTOR

Exudate
|
$(NH_4)_2SO_4$ at 1/3 saturation
|
precipitate
|
treated with distilled water
|
shake
|
insoluble material
|
dialyze until free of SO_4
|
pyrexin (dried by freezing)
|
reflux with 0.1 N HCl for 10–15 minutes
|
cool
|
N NaOH adjusted to pH 10 or 10.3
|
concentrate on steam bath to about 1/10th volume
|
dialyze
|
evaporate to dryness on steam bath or dry freeze
(*leukopenic factor*)

The final material obtained when extracted from pyrexin, as indicated above, still induces a marked leukopenia. This, as in the case of the whole exudate, develops abruptly, and it may last a few hours. The average fall in 14 experiments is 6,146 cells per cubic millimeter, a drop of over 50 per cent. Yet, this leukopenic factor is now essentially dissociated from pyrexin, for it essentially causes no fever when injected into the blood stream of dogs. Preliminary observations in collaboration with Dr. Frederick Bernheim, to be subsequently reported in detail, on the amino nitrogen concentration before and after hydrolysis indicate that the leukopenic factor seems to belong to the group of polypeptides. It is thermostable, for boiling fails to inactivate its effect. Various controls, such, for instance, as the normal variation in leukocyte counts and in temperature level during the period of study (*i.e.* within about 6 hours) or the reagents themselves that were utilized in dissociating the leukopenic factor from pyrexin, all indicate that the effect of the leukopenic factor is indeed real. These studies are being pursued further and will be reported *in extenso* elsewhere.

In brief, evidence has been advanced to indicate that there exists in inflammatory exudates, particularly when obtained from an area of severe inflammation and therefore usually at an acid pH, a leukopenic factor, which *per se* may offer a reasonable explanation for the development of a state of leukopenia with some of the types of acute inflammation. Furthermore, in the exudative material this leukopenic factor seems to be in close association with pyrexin, the pyrogenic factor from which in turn it can to a large extent be separated. The leukopenic factor affects the granulocytes as well as the mononuclear cells, for the latter are likewise depressed. The effect is a general one. The leukopenia is found to exist both in the peripheral circulation and in samples of blood obtained from the heart.

In subsequent studies since this communication was sent for publication, it has been found that, although the leukopenic factor of inflammatory exudate is mostly found in close association with pyrexin, it can be recovered sometimes to some extent in other fractions of exudative material, indicating that it is apparently not exclusively found in association with pyrexin. Furthermore, additional studies seem to indicate that the leukopenic factor of exudates does not primarily deplete the bone marrow, but rather the mechanism involved appears to be a rapid trapping of leukocytes in the alveolar walls of the lungs, in the sinusoids of the liver, and apparently in the spleen. The latter fact may be of significance in our further understanding of the mechanism involved in the acute splenic tumor accompanying numerous inflammatory processes.

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The Comparative Toxicity of Thiourea to Four Mutants of *Drosophila melanogaster* [1]

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During the course of an investigation of the effects of a number of drugs upon the development of several genotypes of *Drosophila melanogaster,* the striking toxicity of thiourea [2] was observed. A survey of the literature disclosed several reports dealing with thiourea as an insecticide. Two-per cent solutions of thiourea and phenylthiourea were effective against the webbing clothes moth (*9*). Third instar blowfly larvae died in the third or fourth instar when exposed to thiourea incorporated in their food (*6*). McGovran, Richardson and Piquett (*8*) observed a 92-per cent

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[2] The authors are indebted to Dr. Stanton M. Hardy, of the Lederle Laboratories for a supply of thiourea.

mortality in the housefly (*Musca domestica*) when third instar larvae were raised on a medium containing 7.5 mg. of thiourea per 23 grams of food. Sixty milligrams of borax were needed to produce the same mortality, and this amount of DDT yielded a death rate of 88 per cent. In another investigation DDT was found to be more effective than a 1-per cent solution of thiourea in reducing the number of emerging flies (*11*). Feeding a mixture containing 10 per cent of allyl thiourea and 90 per cent kaolin to third instar larvae of the silkworm, *Bombyx mori,* produced no unfavorable effects (*1*).

The following is offered as controlled, quantitative evidence of the effectiveness of thiourea in destroying larval diptera.

Experimental Method

Pearl's (*10*) synthetic medium, S-101, modified by changing the agar content from 2.2 to 2.5 per cent, served as the basic food. To this medium thiourea was added to give the desired concentrations (Table 1). The food was poured into 1×4-inch vials to a depth of $\frac{7}{8}$ inch and was yeasted when cool (one drop of a yeast suspension of one cake of Fleischman's yeast per 100 cc. of water was placed on the surface of the food). The cultures were allowed to stand for 24 hours for yeast growth.

TABLE 1

Effect of Thiourea on Mortality of *D. melanogaster*

Conc. of thiourea Mg./100 cc. of food	Ebony		Sooty		Black		Wild-type	
	No. of larvae	Mortality %	No. of larvae	Mortality %	No. of larvae	Mortality %	No. of larvae	Mortality %
12.5	200	100			210	100		
10.0	200	100	200	100	210	100		
8.0	400	97	200	98	400	84	360	75
7.5	210	96			210	85		
7.0	400	98	200	83	400	76	385	72
6.0	400	87	200	84	360	65	360	59
5.0	370	75	200	66	440	58		

Ten newly-hatched larvae were placed in each vial and incubated at 25° ± 0.05° C. The four genotypes, ebony, sooty, black, and Wild-type, were tested in these experiments. The animals were examined at intervals during the larval and subsequent developmental periods.

A number of preliminary runs established that at concentrations ranging from 250 mg. to 20 mg. of thiourea/100 cc. of food all larvae died in the first or second instar. This obtained for dosages of 12.5 and 10 mg./100 cc. of food, with a rare individual reaching the third instar and attempting puparium formation. In the final experiments concentrations ranging from 12.5 to 5 mg./100 cc. were used.

Results and Discussion

Genetic considerations. The data indicate a marked genetic difference in the resistance of these four stocks to the drug, the Wild-type being the most resistant of the four genotypes tested. Black is a II-chromosome recessive mutant, and ebony[11] a III-chromosome recessive mutant from the Wild-type. These two mutants are phenotypically indistinguishable and have normal viability on standard culture media. However, they show a marked difference in resistance to thiourea, black being much more so than ebony. The recessive mutant, sooty, is an allele of ebony and only a slight departure from the Wild-type body color as compared to the black color of the ebony[11] flies. The sooty genotype seems to withstand the drug better than its allele, ebony. This difference may be more marked than the data appear to indicate. The black and ebony[11] stocks were single locus differences from the Wild-type stock, but the sooty stock also carried the mutants, curled wing, stripe, scarlet, peach, roughoid, hairy, and thread—a total of eight mutant loci differences from the Wild-type stock. The cumulative deleterious effects of mutants in compound stocks is well known. It may be that the rather close approach of the sooty mortality to that of its allele, ebony (Table 1), is due in large part to this cumulative effect. If this is so, then the true mortality of the sooty allele is much lower than the figure indicated. This would bring its resistance to the drug more nearly into line with its slight deviation from the Wild-type body color, making the sooty gene both physiologically and morphologically a less extreme variation than the ebony gene from their Wild-type allele. The marked mortality difference between the phenotypically similar black and ebony stocks shows that there must be significant differences in the nonvisible physiological effects of the genes at these two loci. We have observed marked developmental-morphological effects of thiourea at certain dosages. These results are being reported elsewhere. One of us has found different developmental effects of other unrelated drugs on *D. melanogaster* (Harnly, in press). It is evident that the use of drugs might prove a profitable technique in the study of the nature of gene action with *D. melanogaster.*

Thiourea as a larvicide. The numbers of individuals treated and the mortalities of the four genotypes at the indicated dosages are given in Table 1. The mortality values are calculated on the number of emerged adult flies. Examination of the table reveals that a concentration of 12.5 and 10 mg./100 cc. produced 100-per cent mortality in the mutants, ebony, sooty, and black. The trend of the data indicates that a 100-per cent mortality of the wild-type would be produced at some concentration between 15 and 10

mg./100 cc. At lower concentrations of 8–5 mg./100 cc. there was a progressive decrease in the death rate. It is evident that even in concentrations as low as 0.005 per cent thiourea is highly toxic to *D. melanogaster*.

Following recent large-scale field spraying of DDT to destroy mosquitoes, wholesale destruction of fish and other fresh-water life was observed. It should be noted that thiourea has no such lethal action upon fish and amphibia. Immersion of young individuals of *Xiphophorous hellerii* and *Platypoecilus maculatas* in water containing 33.3 mg. of thiourea/100 cc. for periods up to five months resulted in vigorous fish which did, however, exhibit retarded growth and development (*3*). It has been demonstrated that animals (frogs, *4, 5, 7*; and mammals, *2*) retarded by thiourea will resume normal growth and development upon discontinuation of the thiourea treatment. It should be emphasized further that the nonlethal concentration employed in the fish experiment is more than 300 per cent higher than that which yielded 100-per cent mortality in Drosophila larvae.

In view of these facts it was considered worth while to investigate the effects of thiourea upon mosquito larvae. The results of these tests will appear in a subsequent publication.

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News and Notes

Lee A. DuBridge, who returned to the Department of Physics at the University of Rochester in February from the NDRC Radiation Laboratory, Cambridge, has been made president of California Institute of Technology. He succeeds Dr. R. A. Millikan, who retires this spring.

T. Wayland Vaughan, of Washington, D. C., former director of the Scripps Institution of Oceanography, has been awarded the Mary Clark Thompson medal by the National Academy of Sciences. Dr. Vaughan was honored by this award "in recognition of his outstanding achievement in such purposeful and ingenious coordination of observations and generalizations made in and bearing on the fields of stratigraphic geology and paleontology."

Charles B. Fawcett, geographer of the University of London, will be in residence at the Clark University School of Geography during the second semester, February to May 1947. He will offer regular courses of instruction and a series of special lectures during his stay in the United States.

Arthur L. Samuel, of Bell Telephone Laboratories, New York, will become a member of the electrical engineering faculty at the University of Illinois.

Ray G. Daggs has been appointed director of research at the Armored Medical Research Laboratory, Fort Knox, Kentucky.

Jean Brachet, of the University of Brussels, has been appointed visiting professor of zoology at the University of Pennsylvania for the period January to September 1947. He will teach and conduct research in experimental and chemical embryology at the University during the spring term and work at the Marine Biological Laboratory, Woods Hole, during the summer. Thus, graduate students may work continuously with Dr. Brachet during the entire period.

Ernest Laqueur, Institute of Pharmacotherapy, Amsterdam, delivered the Seventh Harvey Lecture of the current series at the New York Academy of Medicine on 18 April 1946. Dr. Laqueur spoke on: "Interrelationships Between Gonadotropic and Sex Hormones."

R. R. McGregor, senior fellow, Mellon Institute of Science Teachers Association on 1 May 1946. Dr. Mc-Industrial Research, Pittsburgh, addressed a joint meeting of the Franklin Institute and the Philadelphia Gregor spoke on "Silicones: Food for Imagination."