Tableau I

Corrélations entre les taux des corps cétoniques (dosés comme acétone) dans le plasma et dans cinq organes (Rats, mâles adultes, $n = 30$)

	1	2	3	4	5	6
1. foie	—	0,37	0,55	0,63	0,63	0,25
2. muscle strié . . .			0,00	0,71	0,77	0,18
3. poumon				0,54	0,37	0,16
4. rein					0,73	0,34
5. cerveau						0,41
6. plasma sanguin .						—

A première vue ces chiffres se trouvent en contradiction avec le schéma admis du métabolisme intermédiaire des acides gras. On estime généralement que le foie est le principal producteur des corps cétoniques, voire le seul capable de les introduire dans le circuit sanguin qui en assurerait la distribution dans l'organisme. Or, le sang donne des corrélations très faibles avec le foie comme avec les autres organes. D'une manière un peu paradoxale, il présente une corrélation à peine significative avec le cerveau qui, pour autant que l'on sache, n'utilise pas les corps cétoniques du plasma. Par contre, il y a plusieurs corrélations statistiquement valables *entre organes*.

A la réflexion, il est facile de comprendre que le «modèle» mathématique compatible avec nos chiffres ne s'oppose point au schéma accepté en physiologie. Mais nos résultats font croire que *la régulation du taux cétonique des organes ne dépend pas des variations du meme taux dans le sang*. Ces résultats peuvent être présentés aussi sous une autre forme qui éclaircit davantage la situation:

Tableau II

Analyse factorielle, méthode centroïde. Coefficients de saturation

	Facteurs		
	I	II	III
foie	0,74	0,29	0,07
muscle strié	0,68	−0,43	0,41
poumon.	0,52	0,60	0,24
rein	0,89	−0,08	0,18
cerveau	0,89	−0,31	0,19
plasma sanguin	0,42	−0,10	−0,24

Selon le premier facteur, le taux cétonique de plusieurs organes pourrait en partie obéir à une cause commune: c'est le cas du foie, du muscle, du rein, du cerveau et, dans une moindre mesure, du poumon. Le plasma sanguin ne présente pas de liaison aussi étroite avec le premier facteur, on peut même concevoir que son coefficient, dans la première colonne, soit un artefact mathématique, car au point de départ il n'y a qu'une seule corrélation significative (avec le cerveau), médiocre en valeur absolue et contredite par ce que nous savons sur le métabolisme des acides gras. Le deuxième facteur donne une saturation élevée avec le poumon, le troisième est manifestement négligeable.

Il est permis de supposer que le taux cétonique des organes est soumis à un mécanisme régulateur commun qui ne coïncide point avec les fluctuations du même taux dans le plasma. Ce mécanisme trouve apparemment un réflet dans le premier facteur centroïde. Sa nature ne saurait être déterminée par une analyse mathématique: cette dernière pose un problème qui appelle une solution expérimentale.

E. SCHREIDER

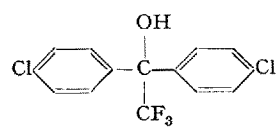
Laboratoire d'Anthropologie Physique de l'Ecole des Hautes Etudes, Paris, le 7 avril 1956.

Summary

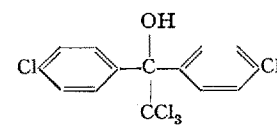
Ketone levels in the rat's organs (liver, muscle, lung, kidney, brain) do not seem to be correlated with the ketone level in the blood plasma. On the other hand, there are significant and high correlations between the ketone levels of different organs. These findings are not inconsistent with the generally accepted theory according to which blood distributes hepatic ketone bodies to the periphery. But ketone levels of the organs seem to be regulated not by variations of the plasma ketones, but by another common factor. At present, it is impossible to say how this regulation is effected.

The Action of Di-(p-chlorophenyl) trichloromethylcarbinol (DTMC) and Di-(p-chlorophenyl) trifluoromethylcarbinol on Houseflies

In course of a research program on DDT-synergists, an attempt was made to reactivate DDT against DDT-resistant houseflies either by keeping DDT residues in a semi-solid[1] or a liquid state[2], or with the help of compounds developed in these laboratories, as e.g. di-(*p*-chlorophenyl) trifluoromethylcarbinol[3] (I). It had been attempted[4] already in 1953 to prepare also the closely related di-(*p*-chlorophenyl) trichloromethylcarbinol (II, henceforward called DTMC). The synthesis of DTMC, m.p. 104–105°C, b.p. 225°/5 mm, has now been realized by chlorination of di-(*p*-chlorophenyl) methylcarbinol (DMC); full details will be published elsewhere.



I



II, DTMC

However, synergization of DDT probably does not represent a solution to the problem of DDT-resistant houseflies, due to (a) the speed of development of resistance to some DDT-synergist combinations[5], (b) reduced synergism in the order solution-, emulsion-, and wettable powderresidues, and (c) the inactivity or very short persistence of DDT-synergist residues against *highly* resistant

[1] S. DAVIDOVICI, Z. LEVINSON, and S. REUTER, WHO/Mal 37 (1950).

[2] K. R. S. ASCHER, S. REUTER, and Z. H. LEVINSON, *Advances in Insecticide Research* (Jerusalem 1951), 18 p.; Chem. Abstr. *46*, 1698 (1952). – K. R. S. ASCHER and S. REUTER, Riv. Parassitol. *14*, 115 (1953).

[3] E. D. BERGMANN, A. S. TAHORI, A. KALUSZYNER, and S. REUTER, Nature *176*, 266 (1955). – A. KALUSZYNER, S. REUTER, and E. D. BERGMANN, J. Amer. chem. Soc. *77*, 4164 (1955).

[4] A. KALUSZYNER and S. REUTER, J. Amer. chem. Soc. *75*, 5126 (1953).

[5] R. B. MARCH, R. L. METCALF, and L. L. LEWALLEN, J. econ. Ent. *45*, 851 (1952).

Table I. — Contact action of 1 g/sq.m. I, 1 g/sq.m. DDT + 1 g/sq.m. I, 1 g/sq.m. DTMC, 1 g/sq.m. DTMC + 1 g/sq.m. DDT, and 1 g/sq.m. DTMC + 1 g/sq.m. DDE on houseflies

4 × 10♀ flies, 2–3 days old; contact – 2 h; t = 27°C																	
R-flies, % k.d. observed																	
	I	DDT + I	DDT	DTMC				DTMC+DDT			DTMC+DDE			DDT		
Age of deposit in days	7	7	7	1	2	7	14	2	7	14	2	7	14	2	7	14
Contact in min																
10	–	–	–	5	–	–	–	–	–	–	–	–	–	–	–	–
20	–	–	–	15	–	–	–	5	2	2	5	2	–	–	–	2
30	–	–	–	20	–	–	–	7	5	2	10	7	–	–	–	2
60	7	–	7	52	5	–	–	37	22	12	65	27	22	–	–	2
90	30	7	10	85	27	17	12	72	50	32	92	47	45	–	–	2
120	55	25	15	87	32	35	30	90	70	52	97	75	70	2	–	10
Σ% k.d.	92	32	32	264	64	52	42	211	149	100	269	158	137	2	0	18

T-flies, % k.d. observed					
	I	DDT + I	DDT	DTMC	DTMC +DDT
Age of deposit in days	7	7	7	7	7
Contact in min					
10	7	25	67	2	20
20	10	85	100	20	90
30	12	90	100	32	100
60	12	90	100	77	100
90	35	100	100	87	100
120	55	100	100	90	100
Σ % k.d.	131	490	567	308	510

Note: No k.d. in untreated controls

strains on *tarsal* contact (unless the synergist itself is a toxicant).

A highly DDT-resistant (R) and a nearly susceptible strain (T) of *Musca vicina* Macq. were exposed to residues from acetone in Petri dishes (continuous contact[6]). Since residues of DDT[7] and of some DDT-synergist combinations on glass tend to stay in the form of droplets (supercooling), R-flies were rushed over the deposits prior to the experiments until crystallization was complete. The results in the Tables are characteristic examples of numerous replications.

Although it has been reported[8] that I is an excellent DDT-synergist when tested by topical application, R-flies, on tarsal contact, were practically unaffected by a residue of 1 g/sq.m. DDT + 1 g/sq.m. I (Table I). The same results were obtained with 0·5 g/sq.m. DDT combined with either 0·05, 0·1, 0·25 or 0·5 g/sq.m. I. In the T-strain, no synergization of DDT by I was evident either, during continuous contact.– I had[9] some slight fumigant properties, which could be demonstrated by a previously described method[9] with some slight modifications (flies above mosquito netting stretched between 2 Petri dish halves of equal size and facing each other, the deposit being on the lower one). R-flies, 2–3 days old, were thus exposed to the vapours only, at 27°C. The following % k.d. was recorded with deposits of 1 g/sq.m. I, 1 day, and 7 days (in brackets) old: 1–8 h: 0 (0); 9 h: 5 (2); 10 h: 5 (2); 11 h: 22 (2); 12 h: 50 (2); 13 h: 52 (20); 14 h: 70 (25); 15 h: 77 (35); 16 h: 85 (47); 17 h: 95 (67); 18 h: 95 (87); 19 h: 100 (92); 20 h: (95); 21 h: (100). The slight action exhibited by I itself on contact (Table I) was thus probably due partly to fumigant properties, which were apparently suppressed by addition of DDT to the residue.

The contact toxicity of DTMC (Table I) towards R-flies is only of very short duration, but its persistence is greatly prolonged by DDT. The enhanced activity of the DDT-DTMC residue (1:1, the same effect was demonstrated with 0·5 g/sq.m. DDT + 1·5 g/sq.m. DTMC and 0·25 g/sq.m. DDT + 0·75 g/sq.m. DTMC) is most probably not due to synergization of DDT by DTMC; it is much more likely that it is a "support"-effect exerted by DDT on DTMC. A similar "support"-effect was obtained, when other DDT-related compounds[10] (either active or inactive), as e.g. di-(*p*-chlorophenyl) dichloroethylene (DDE, see Table I), di-(*p*-tolyl) trichloroethane ("Methyl-DDT") and diphenyltrichloroethane, were combined with DTMC. Moreover, intermittent contact on 7 days old residues (glass jars) gave the following results, when R-flies were transferred after the contact into perforated cellophane bags[11] and observed for k.d. after 24 h:

1 h on 1 g/sq.m. DTMC + 1 g/sq.m. DDT:	52% k. d.
1 h on 1 g/sq.m. DTMC + 1 g/sq.m. DDE:	100% k. d.
1 h on 1 g/sq.m. DTMC, then 1 h on 1 g/sq.m. DDT:	no k. d.
ditto, but *vice versa*:	no k. d.
1 h on 1 g/sq.m. DTMC, then 1 h on 1 g/sq.m. DDE:	no k. d.
ditto, but *vice versa*:	no k. d.
1 h on 1 g/sq.m. DTMC:	no k. d.

DTMC is also much more active against T-flies than I. No synergization of DDT was apparent during continuous contact with this strain, either (Table I). DTMC did not exhibit any fumigant properties.– A closely related compound, di-(*p*-chlorophenyl) dichloromethylcarbinol[12], m.p. 108–109°C, was completely inactive against R-flies on continuous contact.

[6] C. Kocher, W. Roth, and J. Treboux, Anz. Schädlingsk. *26*, 65 (1953).

[7] K. R. S. Ascher and E. D. Bergmann, Bull. Res. Council Israel *3*, 255 (1953).

[8] A. S. Tahori, J. econ. Ent. *48*, 638 (1955).

[9] K. R. S. Ascher, Z. H. Levinson, P. H. Silverman, and A. S. Tahori, Riv. Parassitol. *15*, 45 (1954).

[10] No "support"-effect was obtained with di-(*p*-chlorophenyl) tribromoethane or diphenyl.

[11] F. Beran, Pflanzenschutzber. *11*, 151 (1953). – K. R. S. Ascher and C. Kocher, Exper. *10*, 465 (1954).

[12] J. Pepper and M. Kulka, J. Amer. chem. Soc. *72*, 1417 (1950).

R-flies brought into contact with DTMC or its DDT-"supported" combinations fall on their back and show recurrent tremors of the extended extremities ("Streck-tremor"). Flies kept in contact for long periods often have a blown-up abdomen due to swallowing of air. These symptoms of poisoning somewhat resemble those described for pyrolan[13].

Unfortunately, the action of DTMC and its combinations with DDT and related substances against resistant houseflies, compares very unfavorably with that of the newer phosphor insecticides as e.g. diazinon[6] or malathion (Table II), and it seems that the *insecticidal* properties of DTMC are of theoretical interest only. However, while this work was in progress, excellent *acaricidal* properties were claimed for α-trichloromethyl 4,4'-dichlorobenzhydrol, which seems to be the same compound as DTMC, but neither its mode of preparation, nor any physical properties have been described[14].

Table II. — Contact action of 0·25 g/sq.m. malathion on R-flies

4 × 10♀ R-flies, 2–3 days old; contact – 2 h; t = 27°C					
Age of deposit in days	1	7	14	21	28
Contact in min					
10	32	70	–	2	–
20	90	97	42	10	12
30	97	97	95	62	52
60	100	100	100	100	100
90	100	100	100	100	100
120	100	100	100	100	100
Σ % k.d	519	564	437	374	364

Note: No k.d. in untreated controls

We wish to thank Prof. G. G. MER for helpful criticism.

The excellent technical help of Miss DALIA ROCH is gratefully acknowledged.

S. REUTER[15] and K. R. S. ASCHER[16]

Medical Research Laboratories, Medical Corps, Israel Defence Forces, Israel, April 5, 1956.

Résumé

L'action des carbinols di-(*p*-chlorophenyl) trifluorométhyl et di-(*p*-chlorophenyl) trichlorométhyl (DTMC) a été déterminée sur une souche très résistante de mouches par la méthode de contact. Le premier composé semble agir probablement grâce à de faibles propriétés fumigantes, alors que le second est toxique par contact. L'action toxique de ce dernier est sensiblement augmentée par l'addition du DDT, DDE ou autre composé organique de la série du DDT.

[13] R. WIESMANN and C. KOCHER, Z. angew. Ent. *33*, 297 (1951).

[14] H. F. WILSON and J. S. BARKER, 126th Meeting of American Chemical Society, Section 29A, 1954. – D. ASQUITH, J. econ. Ent. *48*, 329 (1955).

[15] Chemical development of DTMC.

[16] Biological evaluation.

The Effect of Formaldehyde on the Mutagenic Action of X-rays in *Drosophila**

Earlier investigations showed an increase of X-ray induced mutation rates after pretreatment with cyanide and azide in immature germ cells which are characterized by peak sensitivity to the mutagenic action of X-rays[1]. This result suggested that an increased production of hydrogen peroxide, due to inhibition of the cytochrome- and catalase enzyme systems, made the genetic material more susceptible to the effects of radiation. This assumption was further supported by the observation that pretreatment with an organic peroxide (dihydroxydimethyl peroxide) likewise significantly enhanced the mutagenic action of X-rays, notably in the same sensitive stage of spermatogenesis as pretreatment with cyanide and azide[2].

Because formaldehyde is also known to act as a catalase inhibitor[3] and presumably produces mutations via the formation of an organic peroxide[4], it was thought of interest to study the effects of formaldehyde pretreatment on the rate of X-ray induced mutations.

Material and methods.— The formaldehyde used was a BDH commercial preparation. All solutions were made with a 0·7% solution of sodium chloride in distilled water. The formaldehyde concentrations ranged from 0·033–0·050 Mols per litre. 2–3 day old Oregon-K males were injected intraabdominally with 0·28 mm³ of such solutions and were afterwards tested for the incidence of sex-linked lethals by means of the Muller-5 method, the first matings being started one day after treatment. To reduce the time interval between pretreatment and irradiation, the flies were injected in batches of about 30 individuals which were then placed immediately under the X-ray apparatus, the average time interval between injection and irradiation being 11 ± 8 min. The pretreated and X-ray control flies were differently marked with indian ink on the thorax which made possible the simultaneous exposure of both groups. X-radiation was administered by a General Electric, Maximar 100 Model of the Dermatology Clinic of the University of Utrecht. It was run at 100 KVP and 5 mA, at a dose rate of 244 r per min with 1 mm Al filtration (HVL = 1·3 mm Al).

To study the sensitivity pattern in the testes, treated males were remated to 3 fresh, virgin Muller-5 females at specific time intervals. The successive broods arising in this way then represent successively younger stages of spermatogenesis at the time of treatment[5]. No controls were used, because the spontaneous mutation rate in the Oregon-K stock rarely exceeds 0·2–0·3%.

Results.— The results of experiments with 2 different concentrations of formaldehyde are presented in Table I and Figure 1. In experiment 1 pretreatment with a concentration of 0·05 Molar which is hardly capable of raising the spontaneous mutation rate, caused a significant increase of the X-ray induced mutation rates in both the first and second broods. Pretreatment with an even weaker 0·042 M formaldehyde solution in experiment 2 likewise enhanced the mutation rates produced by the irradiation with a factor of from 1·60 to 1·85 in all 3 broods.

* This paper is dedicated to Prof. Dr. JACOB SEILER, Zürich, on the occasion of his 70th birthday.

[1] F. H. SOBELS, Z. ind. Abst. Vererbungsl. *86*, 399 (1955).

[2] F. H. SOBELS, Nature *177*, 979 (1956).

[3] K. G. STERN, Hoppe-Seyl. Z. *209*, 176 (1932).

[4] F. H. SOBELS and J. W. I. M. SIMONS, Z. ind. Abst. Vererbungsl. (in press); Nature *177*, 979 (1956).

[5] CH. AUERBACH, Z. ind. Abst. Vererbungsl. *86*, 113 (1954).