The Toxicity of the Products Formed by the Thermal Decomposition of Certain Organic Substances

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BOTH THE MILITARY services and industry have become increasingly cognizant of the need for toxicological information concerning the products formed from organic substances on contact with metals at elevated temperatures. Accordingly, the immediate toxicity of products resulting from the thermal decomposition of several lubricants, hydraulic fluids, and plastics have been investigated.

In these experiments, the products of thermal decomposition have been more toxic than the vapors or mists of the undecomposed material. Most of the work reported herein has been initiated and sponsored by the Wright Air Development Center, Aero Medical Laboratory, but certain parts of it were sponsored by Monsanto Chemical Company.

It may be of some interest to show that the toxicity of the products arising from the thermal decomposition of a formulated synthetic lubricant which meets the military specifications of MIL-L-7808 is largely that resulting from the breakdown of its principal ingredient, di-2-ethylhexyl sebacate (Fig. 1), and that the presence of a small amount of mixed tricresyl phosphates, the structure of one of which is shown, contributed little or nothing to the toxicity. Of the 10 isomers, the one shown is not present to a large extent, since the tricresyl phosphate was derived from cresols containing less than 3% of the ortho isomer. From a statistical consideration assuming equal rates of phosphorylation, the di-para, mono-meta and the di-meta, mono-para isomers were present in the largest quantity. Furthermore, the toxicity of the products resulting from the thermal decomposition of this formulation is probably somewhat less than twice that of those formed by the thermal decomposition of a paraffinic hydrocarbon lubricating oil.

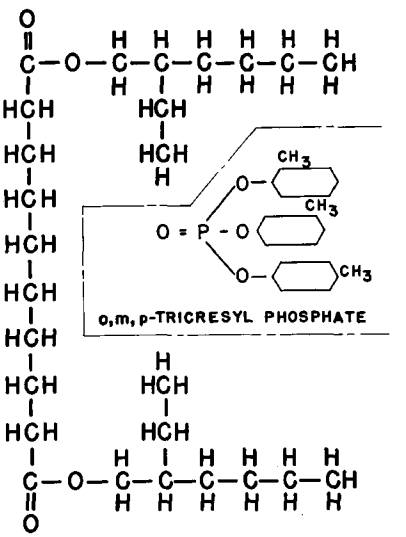

Fig. 1.
Formula for di-2-ethylhexyl sebacate and o, m, p-tricresyl phosphate.

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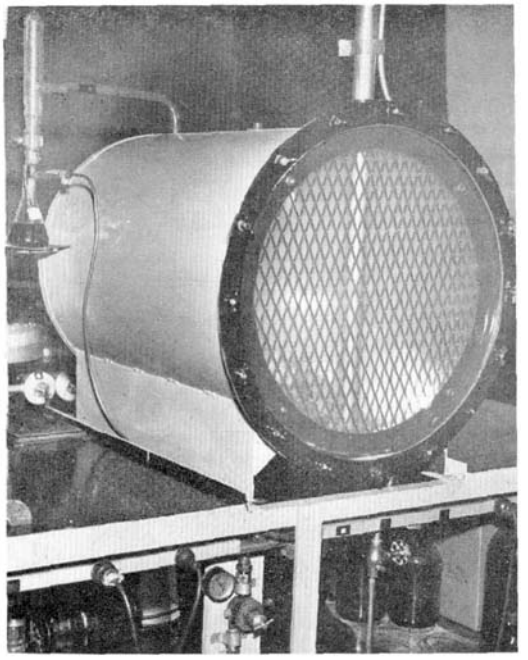

Fig. 2.
Aspirator and 223-liter chamber.

Methods

MISTS were generated by aspiration of the liquids at room temperature, as shown at the left in Fig. 2, by passing compressed air over an orifice,[1] the lower portion of which was immersed in an Erlenmeyer flask containing the material. The intensity of the fog shown in this chamber is of the order of 1 mg per liter (Fig. 2).

The formation of a fog resulting from decomposition of the lubricant at an elevated temperature was accomplished by dropping it at a known rate into an Inconel furnace through the upright tube as shown at the right in Fig. 3. This figure also shows a smaller upright tube to the left through which a thermocouple was inserted into the furnace. Further to the left is shown a condenser coil of Stainless Steel, Carpenter 304, which was immersed in a cooling bath.

Fig. 4 shows a rotameter for measuring the flow of air, the furnace, a semi-potentiometer (for measurement of the temperature of the thermocouple), the cooling bath, the chamber and certain equipment for collecting samples of the atmosphere from the chamber. A schematic diagram of the equipment for generation of a fog at an elevated temperature is shown in Fig. 5.

Results (Esters)

MISTS of either the formulation or of its chief component, di-2-ethylhexyl sebacate, generated by aspiration of air through the lubricant at room temperature, were tolerated by all animals[2] subjected to exposure to concentrations of 1.14 and 0.40 mg per liter, respectively, for seven hours per day on 10 days; however, fatalities occurred among rabbits and rats exposed for only seven hours to the fog resulting from heating the higher of these two concentrations of either the formulation or of its principal ingredient to the temperature of 700°F (Table I).

The mortality in the several groups of guinea pigs exposed to the fog[2] formed by contact of di-2-ethylhexyl sebacate with

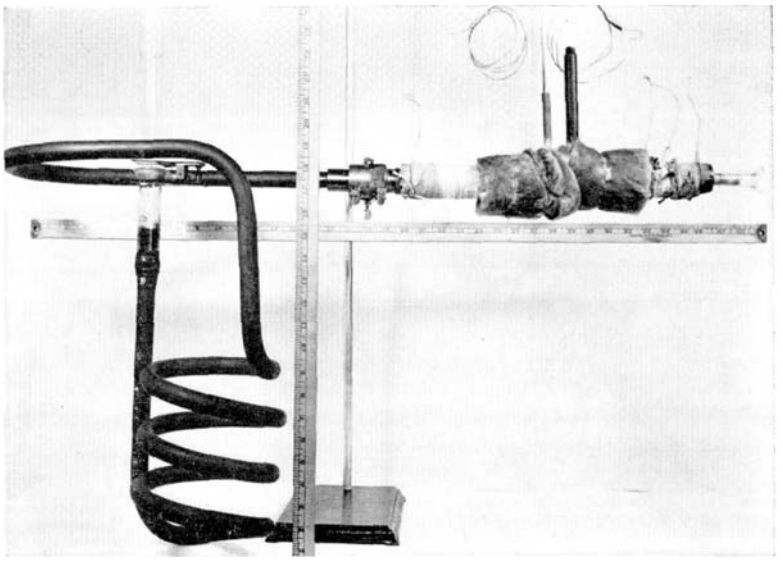

Fig. 3.
Furnace for thermal decomposition and cooling coils.

Inconel at 700°F has been plotted logarithmically in relation to the severity of the exposure in Fig. 6. In this graph, the duration of the exposure in hours has been plotted along the axis of abscissae, and the corresponding rate of delivery of the material in milligrams per minute, along the axis of the ordinates. In all instances, the rate of flow through the furnace was 31.8 liters per minute. The extent to which the circle at a given point is filled indicates the proportion of animals that died under the indicated conditions.

This shows that guinea pigs survived following two hours of exposure, when the sebacate was delivered at the rate of 56 mg per minute (equivalent to 1.76 mg per liter), but that some of them died under otherwise comparable conditions if the rate of delivery was 85 mg per minute (equivalent to 2.67 mg per

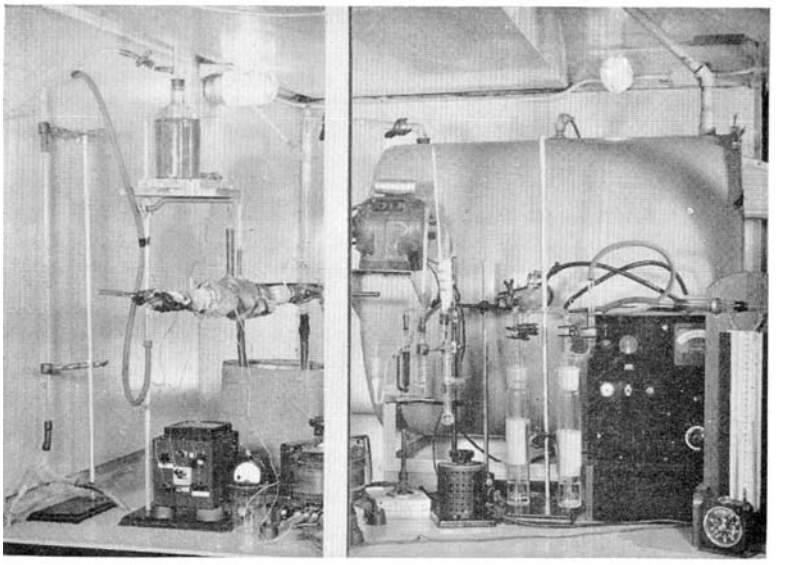

Fig. 4.
Equipment for generation of a fog, chamber and sampling equipment.

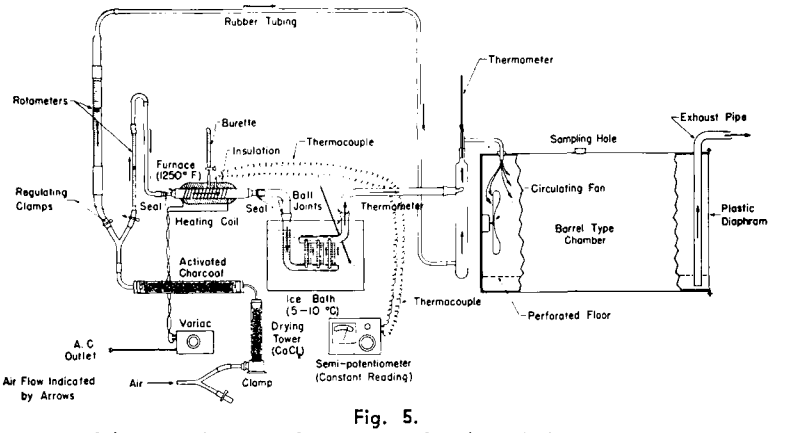

Fig. 5.
Schematic diagram of equipment for thermal decomposition.

TABLE I.
COMPARISON OF THE TOXICITY OF THE MISTS GENERATED BY THE ASPIRATION OF A LUBRICANT AT ROOM TEMPERATURE, AND OF THE FOG FORMED BY DROPPING THE LUBRICANT INTO AN INCONEL TUBE HEATED TO 700°F (371°C.)

Material	Temperature	Concentration of Di-2-Ethylhexyl Sebacate (mg/l)	Duration of Exposure (hours)	Number of Fatalities Per Number of Animals Exposed			
				Cats	Guinea Pigs	Rabbits	Rats
Formulation	Room	1.14[1]	10 x 7	0/1	0/2	0/2	0/2
Di-2-Ethylhexyl Sebacate	Room	0.40[1]	10 x 7	0/1	0/2	0/2	0/4
Formulation	700°F.	0.95[2]	7	—	0/2	2/3	3/4
Di-2-Ethylhexyl Sebacate	700°F.	0.94[2]	7	—	0/2	2/4	3/4

[1]Found by analysis of sample collected from chamber.
[2]Rate of dropping liquid into furnace divided by rate of air-flow (31.8 l per min.) through furnace.

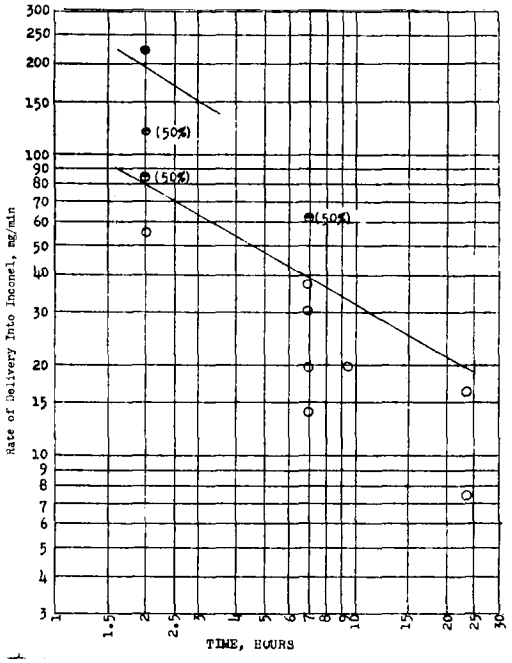

Fig. 6.
Fatalities among guinea pigs following the inhalation of the fog formed by dropping di-2-ethylhexyl sebacate into an Inconel tube maintained at 700°F.

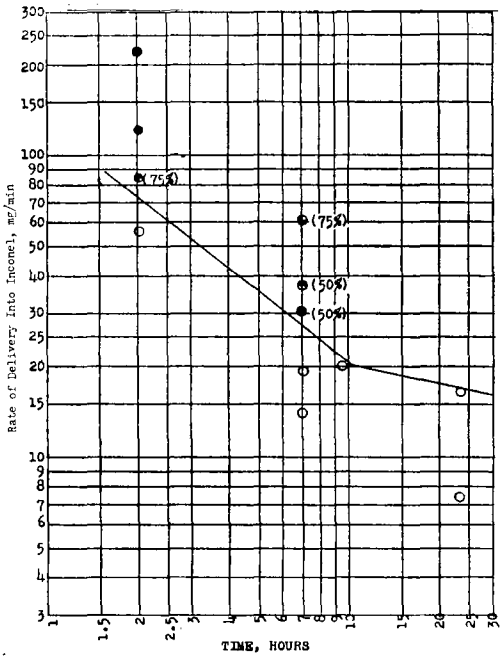

Fig. 7.
Fatalities among rabbits following the inhalation of the fog formed by dropping di-2-ethylhexyl sebacate into an Inconel tube maintained at 700°F.

liter). Likewise, guinea pigs survived following seven hours of exposure when the rate of delivery was 37 mg per minute (equivalent to 1.17 mg per liter) but could not tolerate such a period of exposure when the rate of delivery was 61 mg per minute (equivalent to 1.92 mg per liter). Data obtained on rabbits exposed comparably to the thermal decomposition products of di-2-ethyhexyl sebacate formed at 700°F are shown in Fig. 7, and results of the exposure of rats in Fig. 8. Both rabbits and rats were more susceptible than guinea pigs.

The temperature of decomposition had an effect on the toxicity of the fog formed from di-2-ethylhexyl sebacate. The fog formed at 900°F appears to have been slightly more toxic than that formed at 700°F, while that formed at 600°F differed little in toxicity from that formed at 700°F (Table II). However, when the Inconel with which the material came in contact was maintained at 550°F or 400°F, the fog so created was much less toxic than that formed at 700°F.

In the case of the formulation, greater numbers of comparable experiments were conducted at 700° and 400°F. Under conditions created by the higher temperature, one of 12 guinea pigs died, whereas none of 10 died under those associated with the lower temperature. The fog arising at the higher temperature was lethal to 10 of 17 rabbits, while that formed at the lower temperature resulted in the death of only one of 13 rabbits; 17 of 22 and only one of 20 rats, respectively, died.

The data presented in Table III show that the toxicity of the products of the thermal decomposition of the formulation containing a small amount of tricresyl phosphate was essentially the same as that of the correspondingly decomposed di-2-ethylhexyl sebacate alone. Seven comparable experiments with each of the two substances yielded only minor variations in the mortality among guinea pigs, rabbits and rats. In the case of the guinea pigs, 28% died following exposure to the fog of di-2-ethylhexyl sebacate and 7% died following ex-

thermal decomp almost same 4 base stock and oil formula

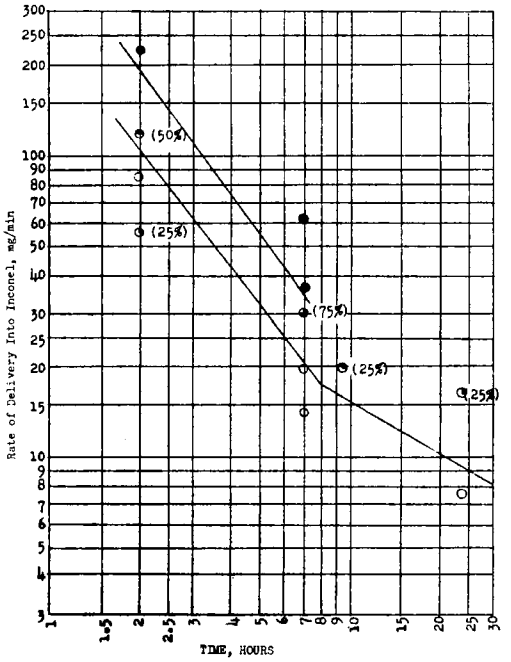

Fig. 8.
Fatalities among rats following the inhalation of the fog formed by dropping di-2-ethylhexyl sebacate into an Inconel tube maintained at 700°F.

posure to the formulation; 44% and 57% of the rabbits, respectively, died and 57% and 54%, respectively, of rats succumbed.

The conclusion that the small amount of mixed tricresyl phosphates contributed little, if any, to the toxicity of the formulation is further substantiated by the difference in the response of guinea pigs to the fogs of either di-2-ethylhexyl sebacate or the formulation, on one hand, and to the fog formed by the thermal decomposition of mixed tricresyl phosphates, on the other. Although the experiments which afford these comparisons were not strictly comparable, in that the temperature at which decomposition occurred was higher (1050°F.) in the case of the phosphates, guinea pigs were more resistant than any other of the animal species to the decomposition products of the ester alone or of the formulation, but they were the most susceptible species to the fog formed from the thermal decomposition of mixed tricresyl phosphates alone. The incidence of mortality among rabbits and rats exposed to the decomposition products formed by the three substances did not differ greatly. In the case of the sebacate alone, five of 24 guinea pigs (20.8%) died; in the case of the formulation, only one of 24 (4.2%) died, but in that of the phosphates alone, 10 of 14 guinea pigs (71.4%) died.

TABLE II.
THE TOXICITY OF THE FOGS FORMED BY THE THERMAL DECOMPOSITION OF DI-2-ETHYLHEXYL SEBACATE AT VARIOUS ELEVATED TEMPERATURES

Temperature of Inconel (°F.)	Rate of Delivery of the Sebacate (mg/min)	Duration of Exposure (hours)	Number of Animals that Died/Number of Animals Exposed		
			Guinea Pigs	Rabbits	Rats
900	82	2.0	1/2	3/4	2/4
700	85	2.0	1/2	3/4	0/4
700	61	7.0	1/2	3/4	4/4
600	58	7.0	0/2	4/4	3/4
700	37	7.0	0/2	2/4	4/4
550	42	7.0	0/2	0/4	0/4
400	36	7.0	0/2	0/4	0/4
		Formulation			
700	20 to 87	7.0	1/12	10/17	17/22
400		7.0	0/10	1/13	1/20

TABLE III.
COMPARISON OF THE FATE OF ANIMALS EXPOSED TO THE FOGS FORMED BY DROPPING DI-2-ETHYLHEXYL SEBACATE OR A FORMULATION CONTAINING IT, INTO AN INCONEL TUBE HEATED TO 700°F (371°C.)

Rate of Air-Flow Through Furnace: 31.8 l/min

Material Added and Rate of Delivery (mg/min)		Duration of Exposure (hours)	Number of Fatalities/Number of Animals Exposed		
Di-2-Ethylhexyl Sebacate	Formulation		Guinea Pigs	Rabbits	Rats
223		2	2/2	3/3	4/4
	207	2	0/2	2/2	2/2
121		2	1/2	4/4	2/4
	129	2	0/2	3/3	2/2
56		2	0/2	0/4	1/4
	60	2	0/2	0/3	0/4
61		7	1/2	3/4	4/4
	61	7	1/2	3/3	4/4
37		7	0/2	2/4	4/4
	43	7	0/2	3/3	4/4
19.8		7	0/2	0/4	1/4
	19.5	7	0/2	0/3	1/4
7.4		24	0/2	0/4	0/4
	7.4	24	0/2	0/2	0/4
Total	Sebacate		4/14	12/27	16/28
	Formulation		1/14	11/19	13/24
Percentage	Sebacate		28	44	57
	Formulation		7	57	54

An ordinary lubricating paraffinic hydrocarbon was decomposed thermally at 800°F. The responses of guinea pigs to inhalation of the products of this heating of both the paraffinic hydrocarbon and the di-2-ethylhexyl sebacate (700°F.) have been plotted in Fig. 9. Attention is called to the relative position of the lower lines for the two materials separating areas of non-lethal exposure from those associated with the death of some but not all of a group. The line for the paraffinic hydrocarbons relates to concentrations about two to 2.5 times those marked out for the sebacate. The upper lines separate conditions which were lethal for some but not all animals, from those which were uniformly lethal. The latter lines are fairly close together.

Similar data relative to the exposure of rabbits to the paraffinic hydrocarbon or to the ester are presented in Fig. 10. The lines separating tolerable conditions from those associated with the death of some but not all of a group are much closer together than in the case of the guinea pigs, the one for the sebacate being only slightly lower than that for the hydrocarbons.

Fig. 11 represents a comparison of the toxicity of the thermal decomposition products of the paraffin with those of the ester, as indicated by the responses of rats. The time-dosage response to the paraffin was more variable than that to the ester. Under relatively mild conditions of exposure, the more susceptible rat is apt to survive after a more prolonged exposure to the fog formed by the sebacate than to that formed by the hydrocarbon; however, on the other hand, under conditions of greater severity, exposure to the fog of the paraffinic hydrocarbon must be more prolonged than that to the fog of the sebacate, in order to kill all of the animals. Thus, if all of the facts are taken into account, the fog of the sebacate is not much more toxic than that of the paraffinic hydrocarbon.

The increasing steepness of the slopes in passing from guinea pigs to rabbits to rats is noteworthy. When the angle of inclination is 45°, concentration and time are equally effective in the determination of these lines. When the angle is less, then concentration is more important than time, and when the angle is greater, time is the more important factor.

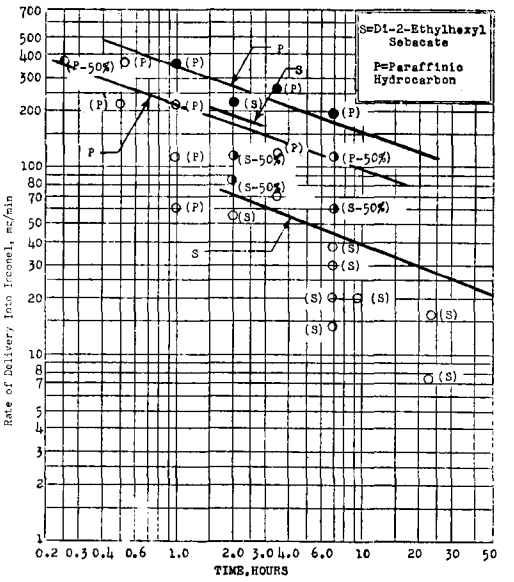

Fig. 9.
Fatalities among guinea pigs following the inhalation of the fog formed by dropping a paraffinic hydrocarbon into an Inconel tube heated to 800°F., or di-2-ethylhexyl sebacate into the tube heated to 700°F.

These fogs produced pneumonitis, and degenerative changes of the brain, liver and kidneys. In the case of the esters and the hydrocarbon, aldehydes, carbonyls, carbon monoxide and undecomposed particulate matter were found in the atmosphere of the chamber. In the case of the tricresyl phosphate, free cresols, undecomposed tricresyl phosphate and carbon monoxide were found.

Results (Halogenated Hydrocarbons)

A SYNDROME similar to that of "metal fume fever" has been reported among men engaged in machining Teflon. This symptom complex has been termed "plastic fume fever."[3,4,5] In view of the dissimilarity in the structure of Teflon and zinc, the extent of the actual difference in their toxic effects is a matter of interest. Is Teflon, when heated, capable of producing the same effects as zinc fume, or does the former induce a more drastic effect and by a different type of action? Graded weights of Teflon-coated copper wire wrapped with an impregnated glass cloth were introduced into an Inconel furnace in which the tem-

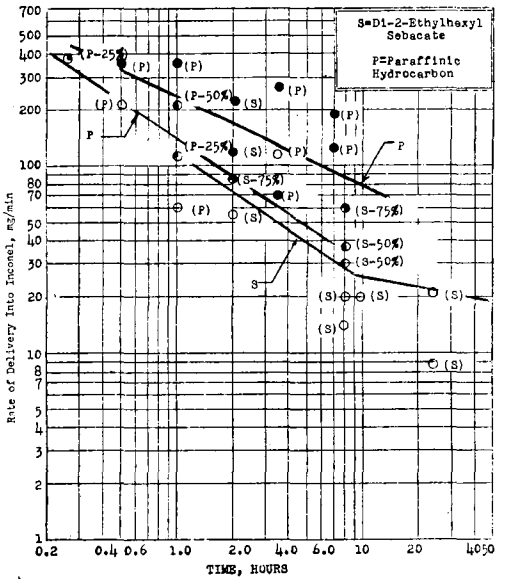

Fig. 10.
Fatalities among rabbits following the inhalation of the fog formed by dropping a paraffinic hydrocarbon into an Inconel tube heated to 800°F., or di-2-ethylhexyl sebacate into the tube heated to 700°F.

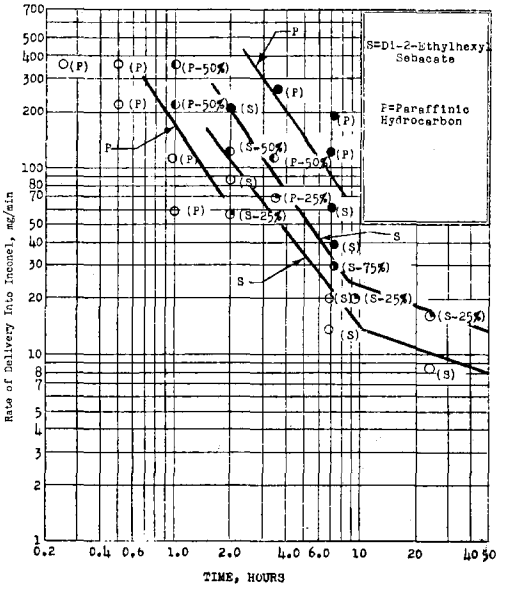

Fig. 11.
Fatalities among rats following the inhalation of the fog formed by dropping a paraffinic hydrocarbon into an Inconel tube heated to 800°F., or di-2-ethylhexyl sebacate into the tube heated to 700°F.

perature was raised rapidly.[6] At temperatures above 400°C. (752°F.) the Teflon appeared to burn rapidly and completely; however, the walls of the furnace were rapidly elevated to a temperature of approximately 800°C. (1472°F.) When animals (Table IV) were exposed for 30 minutes to a progressively decreasing concentration of the fumes formed in the presence of air, the mortality among them varied generally with the amount of Teflon consumed. Cats and dogs, which appeared to be the most resistant of the species of animals employed, died when 14.8 g or more of Teflon were consumed in a stream of 31.8 liters of air per minute, but survived when 6.4 g of Teflon were consumed. Guinea pigs, which succumbed more quickly than other species, tolerated the fumes arising from 1.5 g of Teflon, but some of them died when 3.7 g of Teflon were decomposed. Mice, rats and rabbits were more susceptible to fumes from smaller quantities, deaths occurring among them when only 0.92 g of Teflon was decomposed.

On the basis of a limited number of experiments, the following may be stated:

The presence of the impregnated cloth and the copper wire did not modify the toxicity of Teflon.

Fumes from Teflon heated to 500°C. (932°F.) appeared to be equally as toxic as those formed at 800°C.

Fumes formed from Teflon at temperatures that did not exceed 375° or 390°C. (707° or 734°F.) were much less toxic than those formed at 500°C.

TABLE IV.
MORTALITY AMONG GROUPS OF ANIMALS EXPOSED TO THE THERMAL DECOMPOSITION PRODUCTS OF TEFLON

Decomposition in the presence of air and Cu wire.
Maximum temperature: 800°C.
Duration of exposure: approximately 0.5 hour.

Teflon Consumed (g)	Number of Animals that Died/Number of Animals Exposed					
	Cats	Dogs	Guinea Pigs	Mice	Rabbits	Rats
61.3	1/1	—	4/4	5/5	4/4	6/6
30.0	1/1	—	4/4	5/5	4/4	6/6
15.0	—	—	—	4/5	4/4	6/6
14.8	1/1	1/1	4/4	4/5	1/4	—
6.44	0/1	0/1	4/4	0/5	1/4	6/6
3.72	—	—	3/4	0/5	1/4	5/6
1.51	—	—	0/4	2/5	1/4	6/6
0.92	—	—	0/4	2/5	2/4	3/6

TABLE V.
MORTALITY AMONG GROUPS OF ANIMALS EXPOSED TO THE THERMAL DECOMPOSITION PRODUCTS OF KEL-F

Decomposition in presence of air.
Maximum temperature: 800°C.
Duration of exposure: approximately 0.5 hour.

Kel-F Consumed (g)	Number of Animals that Died/Number of Animals Exposed				
	Cats	Guinea Pigs	Mice	Rabbits	Rats
7.60	1/1	4/4	5/5	4/4	6/6
3.75	—	4/4	0/5	3/4	6/6
1.52	0/1	1/4	2/5	0/4	6/6
0.92	0/1	1/4	1/5	0/4	5/6
0.50	—	0/4	0/5	0/4	0/6

No deaths occurred among animals (five hours of exposure) exposed to fumes of Teflon heated to 300°C.

The fumes formed at 800°C. from 3.6 g of Teflon-coated wire in the presence of nitrogen were at least as toxic as those produced in the presence of air. However, when smaller quantities (0.92 - 1.5 g) were decomposed, those formed in the presence of air appeared to be the more toxic.

Although Kel-F appears to begin to decompose at a lower temperature than does Teflon, the toxicity (Table V) of the fumes formed from the two plastics is of the same order of severity for rats and mice. Rabbits appear to be a bit more susceptible to those from Teflon, while guinea pigs and cats seemed to be more readily affected by those from Kel-F. When Kel-F alone was decomposed in the presence of air (31.8 liters per minute) and the furnace was eventually raised to 800°C., rabbits and cats tolerated the fumes formed from 1.5 g of Kel-F, but died when 3.8 and 7.6 g of Kel-F, respectively, were consumed. Guinea pigs, mice and rats tolerated the fumes from 0.5 g of Kel-F, but some of them died when 0.92 g of Kel-F was decomposed. No fatalities occurred among animals exposed for two periods of five hours to the fumes of Kel-F heated to 200°C.

Animals that died after exposure to the products formed by the thermal decomposition of either Teflon or Kel-F had acute pulmonary irritation (chemical pneumonitis) and diffuse degeneration of the brain, liver and kidneys. The tissues of survivors were normal except for a high incidence of residual pneumonitis and occasionally degenerative changes in the liver. Fig. 12

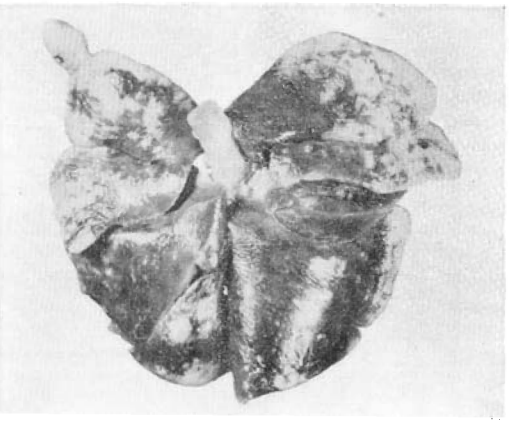

Fig. 12.
Lungs of a dog exposed to the products resulting from the thermal decomposition of Teflon.

Fig. 13.
Lungs of a control dog.

shows the lungs of a dog which died 3.5 hours after being exposed for 41 minutes to fumes arising from the thermal decomposition of 14.8 g of Teflon. Except in the case of certain guinea pigs that died within a few minutes, the hemorrhagic condition of these lungs is typical of the gross effects of the exposure of animals to the thermal decomposition products of Teflon. A picture of the lungs of a control dog is shown in Fig. 13.

In the case of Teflon decomposed in the presence of air, the total strong acids, expressed as HF, were of about the same concentration as the total ionizable fluorides, but when Teflon was decomposed in the

presence of nitrogen the total quantity of ionizable fluorides was several hundredfold greater. Much finely divided particulate matter was present. Bands suggestive of perfluoroisobutene[7] and oxygen difluoride were found in the infrared spectra of the decomposition products of Teflon, but they were not sought in the case of Kel-F. Otherwise, Kel-F gave similar decomposition products. We are indebted to DR. WILLIAM E. KEISER, of the Central Research Analytical Section of Minnesota Mining and Manufacturing Company, for an interpretation of the infrared spectograms.

Summary

THE TOXICITY of the products arising from the thermal decomposition of a synthetic lubricant was derived largely from its principal ingredient, di-2-ethylhexyl sebacate, and only slightly or negligibly from the small amount of mixed tricresyl phosphates contained therein. The toxicity of the products resulting from the thermal decomposition of the formulation or of the sebacate is probably less than twice that of the products formed by the thermal decomposition of a paraffinic hydrocarbon lubricating oil. Fogs formed at 550° or 400°F. were much less toxic than those formed at 600°F. The products of thermal decomposition are much more toxic than the undecomposed material.

The products arising from heating 0.9 g of either Teflon or Kel-F above 400°C. (752°F.) resulted in the death of seven of 19, and seven of 20, experimental animals, respectively. When larger quantities of these plastics were subjected to heat, a higher incidence of mortality, in association with extensive pulmonary damage, occurred among animals which were exposed to the products created by the higher temperature. From the aspect of public or industrial safety, it is evident that caution should be exercised to avoid the storage of large quantities of either Teflon or Kel-F in any vulnerable area, especially in an enclosed space, since in the event of fire large quantities of toxic fumes could be liberated. Masks that protect against acid fumes, organic vapors, and finely divided particulate matter should be employed in fighting fires involving either of these materials.

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Study Industry's Nursing Needs

THE AMERICAN JOURNAL OF NURSING COMPANY recently made a grant to the Minnesota League for Nursing for a two-year study to develop new programs in nursing education, designed to prepare nursing students to meet industry's basic nursing needs adequately. The study will be conducted by six collegiate nursing schools in Minnesota with the cooperation of the State Nurses Association, the Department of Health, and the Board of Nurse Examiners.