Chylomicrons as Carriers for Carcinogenic Hydrocarbons

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Astonishingly little attention has been paid to the physicochemical state in which the water-insoluble carcinogenic hydrocarbons are transported in the body. Although we know comparatively little about the routes and under what conditions, as well as in which form the assumed extrinsic chemical carcinogens enter the living organism, it is—in the study of these problems—most advantageous that the circumstances are as normal as possible.

Observations made on the fate in the body of carcinogenic hydrocarbons applied intravenously as nonnatural (and unstable) suspensions are of little practical significance, or at least the results are difficult to interpret. It is very likely that the carcinogens in real life would not be transported in the form mentioned above. In spite of this, just these methods have, in general, been employed in the studies reported.

Because carcinogenic hydrocarbons are insoluble in water but soluble in fat and fat solvents, it is most likely that their metabolism, especially their absorption mechanism in the body, is linked to that of the lipids in general.

Alimentary fat is transported from the gastrointestinal tract mainly along two routes: to the portal veins and further to the liver, and through the lacteals and the thoracic duct in the general circulation. The physical state in which the main part of the absorbed water-insoluble lipids in the blood stream is transported is that of an extremely finely divided chylomicron emulsion, the average diameter of the particles varying from 0.5 to 1 μ (*1*). The chylomicrons are chiefly composed of neutral fat, the composition of which varies depending on the nature of the alimentary fat (*1–3*). Plasma globulins and albumins make the emulsion stable (*3*).

In our experiments we have observed large amounts of blue fluorescent material in the contents of the mesenteric lymphatics and in those of the thoracic duct in mice and cats after gastric instillation of 3:4-benzpyrene (*4*).

In addition, it has been possible for us to determine that this hydrocarbon or its blue fluorescent metabolites exist in the blood in association with chylomicrons after intestinal absorption of the hydrocarbon, dissolved in fats.

The animals used, about 50 in all, were adult mice of an anonymous known strain employed for several years in our experiments. The dark-field microscope was used; however, instead of the usual visible light, a Philora HPW 125-w mercury vapor lamp served as the light source. Various natural fats and unsaponified liquid petrolatum were used as carriers for the 0.5% hydrocarbon. The use of ultraviolet light considerably decreases the sensitivity of the method, and only a part of the blue fluorescent particles, in Brownian movement, can be distinguished. Because of this, the exact number of the fluorescent chylomicrons cannot be established with certainty with the technique employed in the present work. Therefore, control determinations using the usual dark-field illumination were carried out simultaneously.

After a moderately fatty meal in man, fat in particulate form appears in the blood about 1–1½ hours postprandially, and the maximum is reached in about 3 hr (*1, 2*). In the mouse the postprandial chylomicronemia is practically identical with that in man. Fig. 1 presents the average chylomicrograph in mice.

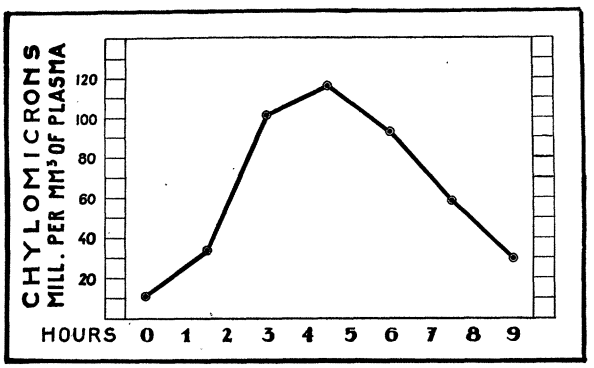

FIG. 1. Normal chylomicrograph in mice.

After a fasting period of about 12 hr 0.05 ml of arachidis oil, containing 0.5% of the hydrocarbon, was fed by means of a stomach tube. The number of the chylomicrons was estimated, using a special counting chamber, which allows quantitative determinations (*2*).

The observations made are not in disagreement with the results reported earlier in the literature when the distribution of hydrocarbons in the blood has been determined by chemical methods or by radioactivity (e.g., *5, 6*), though the results obtained in studies of the "natural" distribution and those reached when artificial, nonnatural suspensions are given intravenously are not per se comparable. The red cells did not contain visible blue fluorescence (*cf. 5*).

Alimentary lipids in the blood can also occur in solubilized state. To what extent and how this happens, has not been established with certainty. The plasma is, as is known, able to dissolve minimal amounts of hydrocarbons, and certain additional factors somewhat increase this solubility.

At all events, depending on their special character, the chylomicrons form a peculiar separate phase in the metabolism and transport of lipids. Under normal circumstances the chylomicrons of the blood are naturally not engulfed by phagocytes in the lung, for instance, as is the fact when nonnatural carcinogenic suspensions are employed: to the latter the organism

reacts as against foreign bodies. The distribution of the alimentary fat into the portal and the lymph system is influenced by several different factors. These have, however, not been sufficiently taken into account in the experimental chemical carcinogenesis with carcinogenic hydrocarbons.

Provided that some carcinogenic agents enter the organism in the diet together with lipids, and bearing in mind the physiologic background, it is possible that additional light may be thrown on the knowledge of the differences, e.g., in geographic and racial occurrence of certain tumors.

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A New Development in the Measurement of High Relative Humidities

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It is often desired to measure high relative humidities in remote and confined spaces. The problem that presents itself here is twofold: First, the sensitivity of most hygrometric instruments decreases rapidly as the relative humidity approaches 100%; second, most standard methods of hygrometry are not applicable to remote and confined spaces. Falling into one category or the other, or both, are such methods as the use of the hair hygrometer, psychrometer, dew-point hygrometer, or the chemical absorption and refractometric methods.

The possibility of overcoming the major difficulties may be found in the electric hygrometer. For obvious reasons an electrical instrument would be especially suitable for remote applications. There are a number of different types of electric hygrometers, all identical in principle: the relative humidity is measured as a function of the electrical conductivity of a hydrophilic chemical. F. W. Dunmore (*1*) has developed an electric hygrometer whose sensitive chemical is a combination of lithium chloride and polyvinyl acetate. The American Instrument Company (*2*) has on the market an instrument supposedly based on that of Dunmore. H. J. Kersten (*3*) has developed an electric hygrometer whose sensitive chemical is gelatin. All these instruments have in common the fact that they are rather small, the dimensions being of the order of a few centimeters. Thus they would be ideal for use in remote and confined spaces.

The sensitivity characteristics, however, vary considerably. It has been found that gelatin is unsatisfactory for the present purposes in that the sensitivity is very poor near 100% relative humidity. Inorganic hygroscopic salts alone are unsatisfactory in that they become wet at high humidities. The combination of an inorganic hygroscopic salt and a hydrophilic colloid, such as used by Dunmore, seems to be the best approach. In the present work lithium chloride and polyvinyl alcohol are used.

The sensitive element consists of a miniature coil form such as is used in radio work, wound with a bifilar winding of #38 AWG platinum wire. Each winding has a pitch of 2 mm, a total length of 3 cm and a diameter of 19 mm. It is important that an inert metal such as platinum or palladium be used for the wire. Metals such as copper or steel produce an aging effect whereby the resistance changes with time.

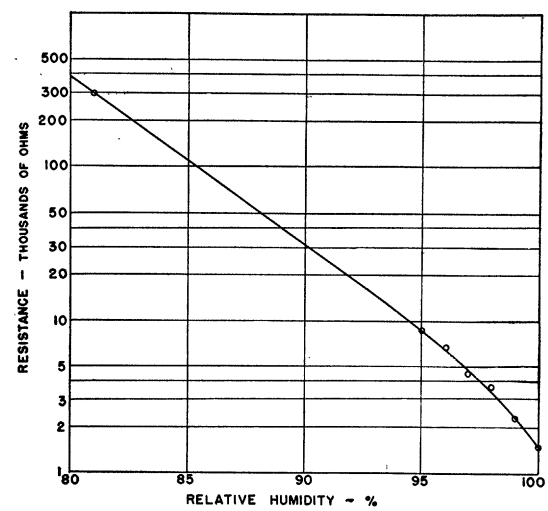

FIG. 1. Calibration curve of the humidity sensitive element.

In the process of producing a sensitive chemical film on the coil, a solution of the chemicals is first made. One part by weight of polyvinyl alcohol in powdered form is mixed with 3 parts ethyl alcohol, producing a viscous, cloudy solution. One part by volume of this solution is diluted with 6 parts of a solvent made with equal parts of water and ethyl alcohol. The still-cloudy solution is allowed to settle for a few days in a well-stoppered bottle. The top clear portion is then decanted, and to this is added 1% of a saturated solution of lithium chloride.

The sensitive film is formed by dipping the coil form into the above solution so that all the wires are covered, and slowly and steadily withdrawing the form, taking about 10 min to withdraw it completely. The element is then stored in a clean, dry place and allowed to "cure" for several days before being used. It was found that this element satisfactorily covered the range from 80% to 100% relative humidity, with a corresponding variation in resistance from 400,000 to 1,500 ohms.

The resistance of the element was measured on an a-c Wheatstone bridge. Alternating current must be

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