# THE SELECTION OF NON-CARCINOGENIC FROM CARCINOGENIC OILS.

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We have now arrived at a stage in our investigations into the carcinogenicity of mineral oils when we feel that a general statement as to the conclusions to be drawn from our results may serve a useful purpose in directing those concerned in the welfare of employees who may be habitually exposed to contact with these substances. From time to time we have published in British and Continental scientific journals the results of our experiments in numerous directions, and at the present juncture we intend to analyse our results as a whole, and to indicate what, in our opinion, is the procedure to be adopted in order as far as possible to eliminate the particular industrial cancers with which we are at the moment concerned.

The recommendations given in this paper are the culmination of the work performed by the scientific staff of these laboratories during the last seven years. All members of the staff have helped us materially by their industry in arriving at a solution of this particular part of our problem which we had set ourselves out to try to solve. We would mention specially our two collaborators Dr A. C. Bottomley and Mr J. M. Twort, and our stewards Mr J. Cox and Mr R. Combes. The recommendations given in this paper must not be considered as final, but we feel confident that they are, at least, in the right direction, and therefore do not hesitate to offer them for the benefit of all interested, although at a later date we shall almost certainly wish to introduce some modifications to our present statements. At the moment we shall deal with prophylaxis only from the point of view of the types of oils to be selected. Shortly we hope to be in a position to give recommendations with respect to prophylaxis by the utilisation of lanolin, etc., and to amplify what we have already said on this subject in some of our scientific publications.

We have divided our subject into three sections:

A. The carcinogenicity of oils;

B. The selection of oils according to origin;

C. The selection of oils according to physical characteristics;

and we shall conclude with a general statement as to our recommendations. We shall only very briefly touch upon the essential points as our scientific publications are already available for those who may wish to be more fully acquainted with the results of individual experiments.

### A. THE CARCINOGENICITY OF OILS[1].

From the experimental and clinical evidence available there appears to be no reasonable room for doubt that contact of the skin of men with certain oils is an important etiological factor in the induction of many industrial skin cancers. We are aware that there are some, admittedly few in number, who deny that there is any evidence in support of the above thesis, but it is not intended in this paper to enter into the relative quality of the logical reasoning of one party versus that of another, but to discuss the matter solely as reason has dictated to us.

Although we have dealt with oils in general it is essentially lubricating oils with which we are at present concerned. For our purpose oils may be conveniently divided into three groups:

(1) Animal and vegetable oils and fats (saponifiable),

(2) Mineral oils occurring naturally in certain geological strata, and

(3) Mineral oils obtained by the destructive distillation of oil shale.

All the animal and vegetable oils tested by us on animals have proved to be incapable of inducing tumour formation during the life of our animals. On the other hand, oleic acid and linoleic acid, unsaturated fatty acids which may be present in commercial saponifiable oils have frequently induced tumour formation; observations which in our opinion are of the highest importance in relation to many cancers other than those of the skin, and possibly even of those of the skin itself.

We view all mineral oils occurring as such in nature as potentially capable of exciting cancer formation with the exception of the white oils. The latter include the lighter boiling "spirits," medicinal liquid paraffin, etc. There is, however, a profound difference in the degree of carcinogenic activity of samples of mineral lubricating oils, some being almost inert while others are very active. This brings us to our third and most actively carcinogenic group, viz. the shale oils. Our animals develop cancer more rapidly when placed in contact with shale oil than when placed in contact with any other oils we have so far tested. In view of their manufacture by the destructive distillation of oil shales it is not surprising that their activity approximates that of many tars, the latter themselves obtained by the destructive distillation of coal.

It has been found that the carcinogenic constituents of a given crude are not equally distributed in the various products of distillation obtained from this crude. The activity of the first products to come over in the still, the motor spirits, etc., is negligible, and that of the lamp oils, burning oils, light fuel, etc., is also of little account, but when we reach the boiling range of the lubricating oils a definite carcinogenic activity may become manifest. Among the latter the most active grades are, on the whole, the spindle grades, closely followed by oils of a Redwood viscosity of 500 to 1500 at 70° F., with a gradual decrease in activity as one approaches the internal combustion engine (motor car)

[1] *J. of Industrial Hygiene*, **13**, 204 (1931); *Amer. J. of Cancer*, **17**, 293 (1933).

grades. The crude oils themselves, as a rule, are somewhat less potent than the motor car oils, but, of course, it will necessarily depend upon the amount of refining to which the latter have been subjected before being marketed.

### B. The choice of an oil according to origin.

The choosing of an oil from the country or field of origin must of necessity be a risky procedure unless we are certain that all oils from one country or field are constitutionally similar. We know, however, that this is not the case, and that a single country may yield oils of widely different character, and therefore potentially of widely different carcinogenicity. It might be assumed from these remarks that the selection of an oil on origin alone is consequently worthless, but we must be careful not to move too hastily. There are several points to be considered. In the first place experiments carried out during the last seven years have shown that there is a definite correlation between the carcinogenic activity of our oils and their country or field of origin as stated by the supplier. The accompanying Table I shows approximately the variation in the carcinogenic activity of the average oils stated to have originated from eleven different oil producing areas. It will be noted that this variation is considerable, and that the variation between individual samples from a single area may be very great indeed, but we must remember that variation in animal susceptibility may be the most important factor in these instances.

Table I.

| Stated origin | Potency | |
|---|---|---|
| | Mean | Extremes |
| Russian | 5·7 | 0·1–30 |
| Pennsylvanian | 9·7 | 1–37 |
| Texas | 10·5 | 1–30 |
| Mid-Continental | 25·2 | 11–50 |
| Mexican | 37·5 | 3–89 |
| Californian | 39·5 | 10–86 |
| Roumanian | 46·5 | 44–53 |
| Persian | 56·0 | 42–82 |
| Borneo | 81·0 | 30–150? |
| Venezuelan | 117·5 | 56–177 |
| Scotch Shale | 227·0 | 179–338 |

We wish to emphasise again here that extreme caution must be exercised in drawing conclusions from the above table. We would particularly point out that

(1) the figures refer of necessity only to our own random samples which in effect may not have represented average samples,

(2) there is a great variation in carcinogenic potency of oils from one and the same country, and

(3) the stated origin may not be the correct origin.

Further we would add that adequate refining of any of the oils we have handled, of no matter what origin, results in a product of good lubricating qualities, possessing only a very low carcinogenicity.

Another point of importance is that in all probability very few of the samples as we receive them are really pure samples from a single well, much less from a single well tapped at a specific level at a specified time. Indeed we have learnt to assume that the majority of our samples of what have been provided as "straight" oils, although correctly designated in so far as the stated area of

origin is concerned, are in reality a mixture of the products of several wells from this particular area. However, from the practical point of view this unavoidable mixing of the oils is of little consequence, it meaning that instead of our testing the carcinogenicity of an oil from a single well we have been testing that of the mean of several wells. In other words, instead of our having tested, for example, the oils from twelve wells of a given area we have in effect tested the mean carcinogenic activity of perhaps the oils from ten wells twelve times: or possibly we have in the mean carcinogenic potencies of the different areas given in Table I arrived at the mean activity of the oils from 120 wells. If this were so our figures become even more impressive.

A third aspect of our subject concerns the attitude of the buyer. He habitually specifies simply as to Sp. Gr., flash and viscosity, and in this case it may result in his purchasing the more carcinogenic types of oils, the market price being on the whole lower than that of the more fully hydrogenated oils. If he wishes to avoid highly unsaturated oils he may specify lower gravity, for he is quite aware that certain low gravity oils are more completely hydrogenated than are many of the other higher gravity oils. The stipulation of a low gravity in his specification will probably, although by no means necessarily, result in his obtaining an oil of lower carcinogenicity than would have been the case had the gravity not been specified. It is better, however, that the buyer who is interested in obtaining an oil which is of low carcinogenicity should specify further than as regards gravity, viscosity and flash, for a low gravity specification would not exclude possible incorporation in his oil blend of the highly carcinogenic shale oils (low gravity) and at the same time it might exclude the incorporation of some of the lowly carcinogenic (high gravity) Texas oils, etc. He should also specify as to origin. The oil industry as a whole is acquainted with the fact that certain areas tend to yield oils which are more completely hydrogenated than are those of some other areas, so that if a buyer specifies as to origin the supplier will be restricted as to the oils he can use for the making up of the specification.

It is to be supposed that the buyer is little interested in the origin of the oil *per se*, but is only concerned with its conforming to his specification. As a matter of fact by the suitable treatment of an oil from one area it may, in some cases, be made to give the physical readings of an oil from a second area, but under these circumstances the carcinogenic activity of the former oil would probably, but not necessarily, approximate that of the latter. It will be gathered from the foregoing that while the buyer may, for example, ask for a Pennsylvanian oil of definite specification he will not be genuinely concerned as to whether the oil really originated from Pennsylvania as long as it conforms to his specification. Nor will it probably matter in that case from the mule spinners' point of view, for in order to bring the oils originating from fields providing more active samples up to the buyer's specification the oils from such fields will in all likelihood have been deprived of much of the dangerous constituents by refining treatments.

We arrive then at the conclusion that the grouping of oils according to their country or field of origin gives a valuable indication to the buyer as to what oils he should utilise on the mule spindles in order to eliminate, as far as possible, the danger of mule spinners' cancer. From the cancer point of view a specification as to gravity, flash and viscosity alone may be made up of good or bad oil. He should specify as to origin, in which case any of the bad group which may be utilised for the making up of his specification will probably have been treated in such a manner as to render them of relatively low carcinogenicity, in many cases probably lower than that of the untreated members of the good group. This brings us to another, and possibly better means of avoiding the dangerous oils.

### C. The choice of oil according to physical characteristics[1].

The determination of the carcinogenic activity of any given oil without the aid of an animal test was at the commencement of our work one of our main objectives. If it were feasible, a physical or chemical test should be cheaper, quicker, and much less laborious than an animal test, and what is of still more importance, it should be more exact. The variation among individual members of a given species of animals is so great that never less than a hundred and sometimes several hundred have to be employed in order to test a single substance. And, as an illustration of the amount of time and labour involved, it may be found necessary to apply the oil to the skin of each animal as many as 200 to 500 times over a period of a year or more in order to ascertain the activity of the oil; and even then our results are only very approximate. On the contrary, the taking of the physical readings of an oil as suggested below occupies but a fraction of an hour of time, and, if necessary, several dozen readings may be made in a single day.

The physical readings we intend to discuss are the refractive index, the specific gravity (density) and the viscosity, together with a combination of the two first mentioned, viz. the refractivity. Readings have been made of all our available oil samples which have already been tested on animals, and of which we have consequently a record of the carcinogenic potency. Our results have been then analysed, first as regards correlation of the physical readings with carcinogenic potency and secondarily a correlation of the former with the stated field of origin. The correlation of the carcinogenicity with the field of origin we have just discussed in Section B (p. 466). We repeat here that our findings obviously can only refer to the particular samples of oils which have been available to us, and that therefore any statements made in this paper, based on these findings, must not be considered as final. We shall now discuss the physical readings in relation to carcinogenic potency, treating them in the following order: viscosity, refractive index, density and refractivity.

[1] *J. of Industrial Hygiene* (1933).

(*a*) *Relation of physical characteristics to carcinogenicity.*

(1) *Viscosity.* An examination of viscosity alone gives us very little information as to the probable carcinogenicity of an oil. The indications in this respect have already been discussed in Section A (p. 465).

(2) *Refractive index.* This test alone may be of some value, provided the oil is reasonably refined, and it may give indications in a definite direction if considered together with the viscosity. Other things being equal the lower the index and the higher the viscosity of refined textile oils the lower the carcinogenic activity.

(3) *Specific gravity* (*density*). The indications obtained from a consideration of gravity alone are confused at the low end of the scale by the shale oils, but in any case to obtain information of much value we must also have the refractive index readings. We can say that spindle oils of a high gravity are on the whole more dangerous than similar grade oils of low gravity; on the other hand we remember the relatively harmless (high gravity) Texas oils, and the very dangerous (low gravity) shale oils. If, however, we correlate gravity (density) with refractive index we shall arrive at what is probably the best means we have at present for the identification of dangerous oils from harmless oils.

(4) *Refractivity constant.* The indications obtained from a consideration of the refractivity of oils is most instructive. The remarks we are about to pass refer solely to mineral lubricating oils as obtained commercially by fractional distillation of the crudes, unless otherwise stated, refining being performed by acid and clay treatment of varying degrees of intensity.

(*b*) *The relation of refractivity constant to carcinogenicity.*

Other things being equal we have found that broadly the lower the refractivity the lower the carcinogenicity and that all our mineral lubricating oils having a refractivity above 5600 are very dangerous, while those with a refractivity below 5450 are harmless from the cancer point of view. The former includes the shale oils and the latter medicinal liquid paraffin, etc. Practically all mineral lubricating oils in commercial use at the present time give readings between these two limits, the manufacture of shale lubricating oils, at least spindle oils, having, we believe, been discontinued. Now we have already stated that really all mineral oils other than white oils must be viewed as potentially having some degree of carcinogenicity, a statement in itself which should preclude the use of mineral oils altogether were we seeking oils totally devoid of danger. But our task is to make the best of a bad job, and endeavour, if possible, to select those mineral oils which should prove the least likely to cause trouble.

We have given in Table II a summary of our observations with reference to 100 selected samples of mineral oils, the oils being grouped according to their refractivity readings. The table is impressive, but it is that of average results,

and when we are confronted with an individual sample the matter is not so simple as one would wish. We cannot grade the oils in this way from the refractivities alone because there are certain relatively harmless oils which have a high refractivity and some dangerous ones of which the refractivity does not rise very high. We have to examine other features of the oils, especially viscosity and gravity. If we do this we find that we are in a position to give definite recommendations. Before, however, we come to our recommendations we must mention shortly the refractivity of oils in relation to their stated field of origin.

Table II.

| No. of samples | Refractivity | Carcinogenic potency |
|---|---|---|
| 7 | Below 5500 | 0·3 |
| 14 | 5500–5520 | 8·5 |
| 7 | 5520–5540 | 12 |
| 16 | 5540–5550 | 23 |
| 16 | 5550–5560 | 49 |
| 14 | 5560–5570 | 65 |
| 3 | 5570–5610 | 88 |
| 5 | 5610–5620 | 150 |
| 7 | 5620–5630 | 186 |
| 1 | 5630–5640 | 338 |
| 10 gravity below 8500 | | Less than 1 |

Table III.

| Stated origin | Refractivity | |
|---|---|---|
| | Mean | Extremes |
| Russian | 5503 | 5500–5506 |
| Texas | 5510 | 5507–5517 |
| Californian | 5540 | 5537–5543 |
| Pennsylvanian | 5546 | 5542–5552 |
| Mexican | 5549 | 5544–5555 |
| Venezuelan | 5558 | 5552–5563 |
| Borneo | 5560 | 5535–5617 |
| Mid-Continental | 5561 | 5555–5566 |
| Persian | 5565 | 5563–5569 |
| Roumanian | 5570 | 5568–5573 |
| Shale (Scotch) | 5621 | 5613–5633 |

(*c*) *The relation of refractivity to stated origin.*

There is a good deal of difficulty here on account of the mixing of the crudes from different fields, etc. There is also the difficulty that a wide diversity of fields may be classified under the name of a single area by the time the sample of oil reaches us, and these difficulties are especially evident as regards certain groups. Perhaps the Mid-Continental Texas group will eventually be found to give the most trouble, the number of oil bearing areas in Texas alone being very great. However, without our considering the exact origin of our oils and relying solely upon the stated origin accompanying the samples, we have found a very definite correlation between the refractivity of our oils and their origin. In Table III we give the average figures of a selected number of oils with the maximum deviation on each side.

## D. DISCUSSION.

Although we have examined only a relatively few samples we feel that we have dealt with a sufficient number for our random sampling to provide us with data of value. There is no denying the fact that among our samples there is a definite correlation between:

Field of origin and carcinogenic potency,
Field of origin and refractivity, and
Carcinogenic potency and refractivity,

and when we have knowledge of any two of the three we usually have not much difficulty, by deduction alone, in coming very near to the third (see Table IV).

Table IV. *Summary of data (mean).*

| Stated origin | Gravity | Refractivity | Potency |
|---|---|---|---|
| Russian | 9055 | 5503 | 5·7 |
| Pennsylvanian | 8901 | 5546 | 9·7 |
| Texas | 9242 | 5510 | 10·5 |
| Mid-Continental | 9125 | 5561 | 25·2 |
| Mexican | 9084 | 5549 | 37·5 |
| Californian | 9317 | 5540 | 39·5 |
| Roumanian | 9276 | 5570 | 46·5 |
| Persian | 9046 | 5565 | 56·0 |
| Borneo | 9454 | 5560 | 81·0 |
| Venezuelan | 9292 | 5558 | 117·5 |
| Shale (Scotch) | 8987 | 5621 | 227·0 |

N.B. It will be seen that we make mention of only eleven of the very numerous geographical oil-bearing areas of the world. This is due to our great difficulty in obtaining authentic samples other than of those habitually distributed in this country.

It must be understood that we are discussing only mineral oils without any addition of a saponifiable oil. The presence of a small amount of the latter would upset our relationships altogether, refractivity being reduced out of all proportion to the reduction in carcinogenicity. Even with mineral oils themselves it would be an easy matter to confuse us by judicious blending; as, for example, the blending of a small quantity of shale oil with medicinal liquid paraffin, but it is hardly likely that one would meet in practice with a blend of this nature. The percentage of wax has also to be taken into account, this substance tending to alter the refractivity in some cases.

Again the selective extraction of oils with solvents might also confuse in some respects, most of our original samples having been straight distillates from the crude. All the extractives we have used have resulted in our obtaining extracts with a very high refractivity figure and residual oils with a corresponding low figure, the carcinogenic potency moving in the same direction as the refractivity. The extractives thus provide us with a valuable means of removing the bulk of the carcinogenic constituents from the distillates, and it seems that among the different extractives tested sulphur dioxide is at least one which may prove suitable for practical application. A single extraction by this method may profoundly lower the carcinogenic activity of a previously very dangerous oil, while a second extraction may render it almost inert. We

see then, that while our experimental results incriminate strongly oils of a specific designation as to country of origin, how important it is to retain the fact that probably it is a feasible commercial proposition to treat oils of any origin whatsoever, or, if one wishes, oils of any degree of carcinogenic activity so that they may be less dangerous than even the very best of the straight oils utilised to-day.

It will be noted that we have avoided any mention of iodine value of our oils so as not to confuse the issue although some of our previous publications indicate the great utility of the test for measuring the carcinogenicity of mineral oils. We ourselves, of course, make use of the iodine value of an oil whenever possible, and as a matter of fact instead of considering the refractivity we rely upon the direct readings of the gravity and the refractive index given by an oil for estimating the probable carcinogenicity. We have presented our results in terms of refractivity for the sake of simplicity although the correlation of refractivity and carcinogenicity may not be quite so good as the procedure we ourselves adopt.

It remains now only for us to give our provisional recommendations, which we show tabulated so as to make our statements as clear as possible to those who may be interested, but before doing so we would again lay stress upon the fact that the oils we are recommending are not totally devoid of carcinogenicity but they should on the whole have a manifestly lower degree of activity than the average oil habitually used in the past. The important fact to retain is that, other things being equal, the lower the refractivity constant of a mineral lubricating oil the lower the carcinogenicity.

### E. Refined mineral lubricating oils recommended.

(1) Refractivity 5560 upwards should be avoided.
(2) Refractivity 5550–5560, see that gravity is very low.
(3) Refractivity 5540–5550, see that gravity is below 895.
(4) Refractivity 5520–5540, see that gravity is below 905.
(5) Refractivity 5510–5520, see that gravity is below 920.
(6) Refractivity 5500–5510, see that gravity is below 930.
(7) Refractivity 5500 downwards, see that gravity is below 940.
(8) Gravity 940 upwards should be avoided.
(9) When selecting from several mineral oils of similar gravity specify that with the lowest refractive index.
(10) When selecting from several mineral oils with similar refractive index specify that with the highest gravity.
(11) When selecting from several mineral oils with similar refractivity specify that with the highest viscosity.
(12) When selecting from origin alone choose in the following order: Russian, Pennsylvanian, Texas, Mid-Continental, Mexican, Californian, Persian, Roumanian, Borneo, Venezuelan, Shale.

In order to simplify matters for both the oil supplier and the oil purchaser, and in order meanwhile to allow of as wide a range of oils being utilised as we consider consistent with a reasonable degree of safety, we suggest provisionally that spindle oils should conform as nearly as possible to the following standard.

"Mule spindle mineral lubricating oils should have a refractivity below 5520 when the specific gravity is above 895, or a refractivity below 5550 when the specific gravity is below 895."

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