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on Carcinogenicity

meeting

MINUTES
SUBCOMMITTEE ON CARCINOGENICITY

CONFIDENTIAL

November 11, 1948

A semi-annual meeting of the Subcommittee on Carcinogenicity was convened at 11:00 A.M. Thursday, November 11, 1948, in Private Dining Room #1 of the Stevens Hotel, Chicago.

MEMBERS PRESENT

L.E. Curtis
T.M. Frank
A.E. Hoag
J.P. Holt
W.R. Levis
M.N. Newquist
C.A. Swan
McIver Woody

L.C. Beard, Jr.
A.E. Dooley
H.G.M. Fischer
H.R. Warrick
H.H. Zuidema

VISITORS

V.C. Baird
W.W. Brooks
F.F. Boys
Kieffer Davis
B.B. Reeves

E.W. Adams
R.C. Cole
N.J. Gothard

GUESTS

Dr. Robert A. Kehoe - University of Cincinnati
Dr. Francis F. Heyroth - " " "
Dr. A. Wesley Horton - " " "
Dr. W.D. Seyfried - Humble Oil & Refining Company
Dr. S.S. Shaffer - " " " "
Dr. H.W. Stevenson - Shell Petroleum Company, Ltd., London
Dr. W.J. Sweeney - Standard Oil Development Company

Total in Attendance - 28

MEMBERS ABSENT

T.J. Kelly

R.S. Bonsib
A.J. Koewing, Jr.
H.P. Lankelma

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The new members and guests, L.F. Curtis, C.A. Swan, R.A. Kehoe, Francis F. Heyroth, A.W. Horton, W.D. Seyfried, S.S. Shaffer, H.W. Stevenson, W.J. Sweeney were introduced.

Dr. Kehoe reported on the status of the experimental studies at the Kettering Laboratory and pointed out the desirability of:

- 1 - Facilities adequate to select materials needed to be tested.
- 2 - Means whereby samples could be studied as to their relative potencies.
- 3 - Systematic data on the incidence of malignancy in petroleum workers exposed to these materials.

As to the progress of the building program at Cincinnati, he said that the new wing originally scheduled for completion in May 1948 would surely be ready for occupancy by March 1949 and would include a special animal house on the roof, which has been designed for mice and other small animals which are used in cancer studies. He reminded us that this additional space and the equipment to be installed therein was made possible by the recent A.P.I. grant for capital expense and he assured us that this space, or its equivalent elsewhere in the building, would be reserved for our work.

Dr. A. Wesley Horton, who has just been appointed as Assistant Professor of Industrial Hygiene, was introduced by Dr. Heyroth, who explained that his entire time would be devoted to our problem. In making this appointment, they have selected an organic chemist with practical experience in polycyclic compounds, a knowledge of physical chemistry and an understanding of our industrial problems and technical processes.

Dr. Kehoe said that their new Professor of Preventive Medicine, who is one of the three outstanding epidemiologists in the country, will be able to devote half his time to the A.P.I. project during the coming year.

Dr. Heyroth then reported on the results of tests of the eight A.P.I. samples. His report and charts will be reproduced and distributed to members of the Committee.

Dr. Holt recommended that a wider range of samples be studied, especially those in the higher boiling ranges (above 700° F) and that waxes be investigated also. He cited an article in the N.Y. Times of November 7, 1948 and said that Standard Oil (N.J.) will cooperate fully with the U.S. Public Health Service in its activities in this field. Jersey has found that, if the heavy oil is diluted with 71% white mineral oil, the activity is reduced to about one-fourth its original potency.

Dr. Newquist referred to recent statements in the literature which say that any skin tumor should be considered as potentially malignant.

Dr. Frank thought it would be desirable to study the effects of these oils following repeated applications and washings, thus simulating the actual exposure of employees.

Dr. Hoag read a report prepared by the Metropolitan Life Insurance Company on "Statistics on Cancer Among Workers in the Oil Industry". He also suggested that some ways be found to challenge incorrect newspaper articles; for example, a recent statement referring to paraffin wax as being carcinogenic.

Dr. Beard read a letter from Col. Auld of the Institute of Petroleum (England) and suggested that Col. Auld be invited to attend a future meeting of the Medical Advisory Committee and describe the work being done in England.

Dr. Stevenson explained that any information given Col. Auld on the problem in the United States would be considered confidential; that the Institute of Petroleum was similar to the A.P.I.

Mr. Warrick stressed the desirability of finding out more about the formation of carcinogens and urged that the technical advisers meet soon with Dr. Horton to discuss these matters.

Mr. Zuidema asked that a comparison between catalytic cracked and thermal cracked material be made.

Dr. Kehoe and Dr. Heyroth, in discussing future work, advocated:

- 1 - Careful consideration in selecting samples for future testing, taking into account the source, the nature of the crude, the temperature conditions, etc. This should be considered by Dr. Horton and the technical advisers.
- 2 - The collection of epidemiological data by an expert in that field. While laboratory methods can determine the relative carcinogenicity of various materials, the final answer will depend on human experience.
- 3 - Study of the reproducibility of results and the effects of dilution.

The following report to the Medical Advisory Committee was approved:

On behalf of the Subcommittee on Carcinogenicity, I present to the Medical Advisory Committee for transmittal to the Safety Committee of the Board of Directors and for adoption by the Executive Committee of the Board of Directors, the following report and recommendations:

- 1 - That the selection of Dr. A. Wesley Horton for Dr. Kehoe's staff is acceptable to us.
- 2 - That the selection of the epidemiologist for Dr. Kehoe's staff is acceptable to us.
- 3 - That an additional \$25,000. will be necessary to continue the program at the University of Cincinnati during 1949 to be followed by another \$25,000. for the first six months of 1950.

- 4 - That the fundamental chemical and physical studies that are indicated to investigate the operational technical aspects of this problem may require considerably more money than anticipated; and it is recommended that the technical advisers group consider the problem again and present their recommendations to the Subcommittee on Carcinogenicity.
- 5 - That the carcinogenic program which the American Petroleum Institute is sponsoring at the University of Cincinnati should include:
 - (a) Biological testing program to determine the carcinogenicity of various samples.
 - (b) Biological or other experimental studies for the purpose of developing quicker techniques for determining the carcinogenicity of these materials.
 - (c) Experimentation directed toward defining protective procedures that might be used to protect individuals who may come in contact with these oils.
 - (d) Epidemiological studies of this problem in the industry.
 - (e) (Deleted by the Medical Advisory Committee).
 - (f) Investigation of solid and semi-solid natural petroleum constituents such as red wax.

McIVER WOODY, M.D.
CHAIRMAN

A.E. Dooley
SECRETARY

Statistics on Cancer Among Workers in the Oil Industry
(Prepared by the Metropolitan Life Insurance Company
at the request of Dr. Hoag and Mr. Beard)

We have reviewed the mortality studies available to us and have canvassed the literature on the subject of cancer among workers in the oil industry. So far as general mortality from cancer is concerned, the evidence indicates that the death rate for oil workers is probably no higher than the average. Gafafer's report on the occurrence of cancer among employees of an oil refinery published in Public Health Reports for August 23, 1940, to which Mr. Beard refers in his letter of May 26th, shows that the crude death rate for the oil workers was no higher than average. We have calculated the expected number of deaths among these oil workers ages 15 to 69, on the basis of death rates from cancer by ages prevailing among white males of the general population in the years 1933-1938. The calculated number of deaths expected for the six year period was 52.6, whereas there were actually only 46 deaths. Some information is given on cancers by site in the original article. Employees of the oil refining company show relatively more cancer of the digestive system than occurred among the adult male population, while the proportion of cancers of the genito-urinary system is somewhat less. We wrote to Dr. Gafafer to see if he had additional information for a more recent period, but he advised us that the 1940 report is his latest.

Some years ago we looked into the Group insurance experience in this matter. In the combined experience of six of the leading companies issuing Group insurance in the United States and Canada from 1927-1932, the mortality from all forms of cancer among all insured workers in the mineral oil industry regardless of the exact occupation, was 36 per 100,000 years of life exposed as against 62 per 100,000 among all of the general occupation group in which those in the oil industry have been classed. Detailed data by cause of death are not given in recent Intercompany Group reports.

Ordinary Department mortality experience is limited so far as cancer among oil workers is concerned. However, while we cannot calculate the ratio of actual to expected deaths from cancer among them, the facts presented in the Joint Occupation Study, 1928,* indicate that in a group of oil and gas field foremen and miscellaneous operatives represented by 51,000 life years of exposure, the cancer mortality was average or below average.

Our Industrial Department experience is quite limited, and the results are out of line with other studies. The number of deaths is so few, however, that the results are not significant. In the period 1937-1939, the standardized relative index for cancer among oil refinery workers, calculated in the manner outlined in our paper, "Occupational Mortality Experience of Insured Wage Earners," was 120, based on 15 cancer deaths; the standardized relative index for the years 1922-1924 was 130, based on 13 deaths.

There is a considerable literature on the occurrence of skin cancers among workers in the oil industry. The best reports of which we have a record are listed on the accompanying sheet. Particular attention is called to the work by Schwartz, Tulipan and Peck.

*Published by the Actuarial Society of America and the Association of Life Insurance Medical Directors.

SELECTED REFERENCES

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Occupational neoplastic disease. The American Journal of Cancer, Vol. XV, April 1931, p. 641.

Heller, Imre

Occupational cancers. The Journal of Industrial Hygiene, May 1930, p. 169.

Henry, S.A.

Occupational cutaneous cancer attributable to certain chemicals in industry. British Medical Bulletin, Vol. 4, No. 5-6, 1947, p. 389.

Hueper, W.C.

Occupational tumors and allied diseases. Charles C. Thomas, Publisher. 1942. p. 896.

Phillips, Charles

The relationship between skin cancer and occupation in Texas: a review of 1569 verified lesions occurring in 1190 patients. Texas State Journal of Medicine. January, 1941, p. 613.

Schwartz, L., Tulipan, Louis, and Peck, S.M.

Occupational diseases of the skin. Chapter XVI - Dermatoses caused by petroleum. p. 232. Lea & Febiger, Philadelphia 1947.

U.S. Public Health Service

Disabling morbidity, and mortality from cancer among the male employees of an oil refining company with reference to age, site, and duration, 1933-38, inclusive, by William M. Gafafer. Public Health Reports, August 23, 1940, p. 1517.

EXCERPTS FROM COLONEL S. J. M. AUID'S
LETTER OF AUGUST 6, 1948

" The subject of the relationship of petroleum to industrial carcinoma and indeed to cancer in general has developed rapidly during the last year or so and appears to be taking on an importance which may seriously affect the nature and provision of mineral oil products and therefore warrants our close attention from those aspects as well as from the serious pathological outlook which is concerned.

" During the early part of the war the matter was relatively quiescent, but came to the front again in respect of the alleged carcinogenicity of textile oils because of further work by Twort and the official adoption of the Twort "safety" formula based on a specific refractivity relationship. Special oils were set aside by the Petroleum Board in order to permit this formula to be met, but at the same time, and possibly due to the traversing of the Twort work from different sources, a movement was made to apply a test in vivo which related carcinogenic activity to change in refractive index of oils injected into the living animal.

" Towards the end of 1943 the matter suddenly came into still greater prominence, via the Ministry of Labour, both in connection with the provision of mule spinning lubricants and the use in increasing quantities of petroleum extracts as replacements for products of different types which were in short supply, particularly rubber extenders and drying oil substitutes.

" As a result, the Petroleum Board, through its Technical Advisers, embarked on biological work in the Pathological Department of the University of Birmingham for the express purpose of developing the whole subject on a reliable basis of observation. Around the same time discussions were started between the various Ministries and Government Departments concerned, representatives of the Spinners' Operatives (the trades unions), the Master Spinners, and the Petroleum Industry. At these meetings the representatives of the Oil Industry were Mr. J. A. Oriel of the Shell Company and myself. One of the matters thereby brought into consideration and now coming to a head, was the suggested adoption of technical white oils as textile lubricants.

" At a recent meeting the significance of this movement was closely canvassed and the Petroleum Representatives pointed out that whilst the research work subsidized by the Oil Industry had in successive reports indicated the biological inactivity of so-called technical white oils, it was necessary to express a warning that their adoption should not be regarded as the final step in either the investigation or the practical consideration of the occupational carcinoma concerned. Indeed, recommendation of the adoption of near white oils, wherever workers were subject to direct contact with petroleum products, might be misleading and dangerous because of the assumption that nothing else needed to be done.

"Moreover, the question of supplies, costs, etc., might render the situation impracticable. It might be far more important to develop the use under such conditions of solvent-treated oils of low biological activity combined with special attention to the avoidance of oil dispersion and to personal cleanliness.

" With the demergence of the Petroleum Board arrangements have been made for the research work, such as that at Birmingham, to be continued under the supervision of the Institute of Petroleum with funds bequeathed by the Petroleum Board and likely to be added to as required by the individual Oil Companies in the future. In accepting this responsibility the Institute of Petroleum appointed a special Research Group which has been placed under my Chairmanship and includes representatives of the major companies and certain University workers.

" Within the last month, quite separately, the Medical Research Council - a body of the highest standing and working directly under the Privy Council on grants allocated by the Treasury, has decided to investigate fully the question of the carcinogenicity of Petroleum Products. In this connection Sir Edward Mellanby, the Chairman of the Medical Research Council, has approached me as representing the Institute of Petroleum for the purpose of effecting contact and establishing co-operation with the Petroleum Industry in general and the I. P. Research Group in particular. From our conversations it appears that such collaboration will be arranged.

" I am informed that the Medical Research Council's interest in the subject has not developed from the textile considerations known to you but largely from observations made by the Medical Officers of the Government Factory Department indicative of dangerous and fairly widespread symptoms arising from the use of certain mould oils in Scotland and from work carried out on automatic tool operatives in the Midlands because of similar or allied occurrences presumably arising from contact of workers with cutting oils.

" The organization proposed by the Medical Research Council will be of a high standard and will bring in all the specialists in allied spheres of work in the United Kingdom. It is intended that the investigations shall be laid out as a succession of long-term projects. It is thought probable, however, that the ad hoc research work on which the Institute of Petroleum Research Group is prepared to embark may well fit as a particular phase of the bigger investigation.

" The Petroleum Industry here has noted with great interest the growing concern of the A.P.I. in the cancer problem in relationship to oil.

" It seems, therefore, of great moment that steps should be taken to correlate the work in the two countries not only to assist in the prosecution of the pathological investigation but from the broader important practical outlook of the Petroleum Industry in its relationship to health."