Review and Commentary on the Seminar on The Biology of Talc Used in Health Products, held at the MRC Pneumoconiosis Unit in Penarth, Wales, May 13 and 14, 1976

The seminar was held at the British Government's Medical Research Council Pneumoconiosis Unit in Llandough Hospital, Penarth, Wales, to review modern scientific data developed on cosmetic grade talc with experts in the field (see attached list of attendees), members of the MRC Pneumoconiosis Unit, representatives of the British Toilet Preparation Federation, and Johnson & Johnson personnel from the U.S.A. and the U.K.

Object of the Meeting

The objectives of the meeting were:

1. To confirm with experts in the field of pulmonary dust diseases that cosmetic grade talc as normally used is not a hazard to health.

2. To identify what if any further studies should be conducted with cosmetic grade talc to consolidate the available data on it.

3. To educate European participants at the meeting on the data supporting the safety of cosmetic talc so that they can confirm the safety of talc with health authorities in Britain and other European countries.

4. To inform experts in pulmonary dust diseases of recent talc studies so that they can act as consultants for industry when needed.

Review of the Content of the Meeting

Although a complete transcript of the meeting will be available from the taping of it, a review of some of the highlights of the meeting is submitted.

The agenda of the meeting (see attached) was designed to review the most recent data on the biology of cosmetic grade talc and allow for appropriate discussion of each paper presented.

The meeting was chaired by Dr. J. C. Gilson, who is the Director of the MRC Pneumoconiosis Unit.

Introduction to the Meeting

Dr. Gilson expressed appreciation of the opportunity for those present to review all available modern data on cosmetic grade talc. He indicated his concern for the current neurosis that exists in the world about health care matters and the unfortunate need to obtain extensive data on materials that have had wide usage. He indicated that the meeting was to review in depth the available scientific data on cosmetic talc and determine what further studies may be needed.

Presentation #1

Composition of U.K. and U.S.A. Commercial Cosmetic Talcs

Dr. Pooley initially reviewed the genesis of talc, the nature of inclusion minerals and the contaminants that occur with talc. He submitted data on the composition of cosmetic talcs that he had analyzed and indicated that they consisted of about 90% talc often associated with quartz, chlorites and carbonates, and occasionally amphobole minerals, but never with chrysotile. It was indicated that substitution of the magnesium within the talc lattice occurs but the substitution would be of limited biological importance as the surface of the talc molecule was biologically inactive and the substituted mineral would be within the lattice. He indicated that the fibers in talc that were important were those of small diameter and that a fiber should be defined as having at least a 20:1 ratio.

The U.S. definition of cosmetic grade talc was discussed, as was that for the U.K., and it was generally agreed that the definitions were comparable and acceptable to industry.

Presentation #2

Talc Dust Concentrations Associated with Cosmetic Usage and Their Relation to Animal and Human Talc Studies

Dr. F. R. Rolle, of Johnson & Johnson, presented data on the dust concentrations used in the reported animal and human talc studies and how they related to the amount of talc to which babies are exposed. The data showed that in those studies where talc showed no effect in animal or human studies the following safety factors existed:

1. The hamsters in the Battelle inhalation study were exposed to 1,375 times the amount of talc to which a baby is exposed per unit of time.

2. Italian millers were exposed in each one year to 12,000 times the amount of talc to which a baby is exposed in a one year period.

3. No cancer was reported in the MRC rat study, although some fibrosis was observed in the rats exposed to 4,339 times the amount of talc to which a baby is exposed in a unit time.

4. No increase in cancers was noted in miners exposed to 120,000 times the amount of talc to which a baby is exposed in one year.

The importance of the safety factors was stressed as they give a real indication of the safety of exposure to cosmetic talc and are facts readily understood by both scientists and lay people.

Presentation #3
In vitro Effect of Talc on Cells

Dr. A. C. Allison, of the MRC Clinical Research Center in Harrow, presented in vitro data on the effect of talc on blood macrophages which was assessed by measuring the release of enzymes. Dr. Allison was interested primarily in determining the fibrogenic property of quartz and is attempting to isolate the mediators of fibrogenesis produced by quartz. He was only interested in evaluating the cytotoxic and fibrogenic properties of talc and was not concerned with evaluating its carcinogenic potential. Quartz was cited as having a highly active cytotoxic and fibrogenic action, and it was Dr. Allison's opinion that talc possessed fibrogenic and cytotoxic properties but of a much lower order than quartz. He indicated that the activity of the talc was dose-dependent. He did not think that the quartz content of up to 2% in the Italian talc was responsible for the biological activity of talc and thought that perhaps another component in the talc was responsible for the data obtained. It was also pointed out that talc did not appear to influence the immune system or produce an immunological response. In the discussion it was mentioned that a separate independent study of the effect of talc on rat pulmonary macrophages had shown that talc did not have a cytotoxic effect nor impair their phagocytic action.

Presentation #4
The Biological Activity of Talc - Review of Past Animal Studies

Dr. G. H. Lord, of Johnson & Johnson, made an extensive review of past animal studies in which talc was utilized and pointed out that in all

but the most recent studies no data were available concerning the dose or the type of talc that was used and as such the studies were of little value. He reported on a study conducted by the F. D. A. in which talc was found not to produce mutagenic or teratogenic activity in the studies conducted. He indicated that all available data reviewed failed to show that talc was a carcinogen.

Presentation #5

Chronic Cosmetic Talc Inhalation Study Conducted in Hamsters

Dr. A. P. Wehner, of Battelle Pacific Northwest Labs., reviewed the findings of an inhalation study conducted in hamsters in which animals were exposed to Vermont talc in doses up to 1,375 times the amount to which a baby is exposed on a unit time basis. He reported that no abnormal findings were observed in any of the treated animals when they were compared with the untreated control group. He also reported preliminary data concerning pulmonary clearance studies utilizing radioactive talc which were conducted in hamsters to determine the fate of talc inhaled by these animals. It was pointed out that half the talc inhaled by the animals was eliminated from the lungs in 8 days and none found in the lungs 100 days after inhalation of the talc.

Presentation #6

Review of Talc Toxicological Studies Conducted in Rats

Dr. J. C. Wagner, of the MRC Unit, said that the objective of the animal studies conducted at the Unit was to determine whether talc was a carcinogen. The design of the inhalation studies was related to the talc exposure encountered in industry and, accordingly, high doses of Italian talc were utilized. The data showed that a low order of pulmonary fibrosis occurred in the animals, although the dose used was 4,339 times that to which a baby is exposed in a unit time. Intrapleural injection of talc and oral ingestion produced no cancers. The degree of fibrosis observed in the inhalation study was dose-related and comparable to that obtained with asbestos. The data showed that talc did not produce mesotheliomas and there was no evidence to show that talc produced cancer when inhaled.

Presentation #7

Review of Findings from a Prospective Study of Vermont Talc Mine Employees

The objective of this study was to assess the health and pulmonary function of talc mine employees on an ongoing basis to see if there were any changes noted in data recently obtained when compared to data obtained

from the miners on a previous occasion. The data presented in this prospective study showed that pulmonary function and health data obtained from miners who do not smoke showed no abnormal changes over the periods that they have been studied. In miners who smoked, however, there was an increase in pulmonary symptoms. The significance of the pulmonary symptoms was considered to be related to smoking and the significance of the changes was not known.

Presentation #8

Retrospective Study of the Cause of Death of Talc Miners and Millers

Dr. G. Piolatto, of the University of Turin, Italy, presented data on a mortality study of miners and millers who had worked in an Italian talc mine and compared the results with data obtained from the Italian male population as a control group. The control data obtained from national data were used in addition to the original control data obtained from the mortality findings in a population living in a rural city. The reason for using the second population was to confirm the initial observations reported by Dr. Rubino. Results of the analysis of data comparing the mortality of the mine employees with the Italian population showed that the data were essentially the same as those obtained where the control group was a rural population. The researchers were commended for their work in obtaining comparative data from the Italian population which confirmed their initial findings.

Presentation #9

Retrospective Study of Patients Treated Intrapleurally with Talc

Mr. G. Berry, of the MRC Pneumoconiosis Unit, described the design of a study that was being conducted by the MRC Unit to determine whether talc introduced in the pleural cavity produced cancer. The study consisted of identifying patients from a hospital near Cardiff and two hospitals in London who had been treated for collapsed lungs with the introduction of talc into the pleura. Records of 62 patients treated in a local hospital were located showing that 2 to 5 grams of iodized talc was administered intrapleurally during the period from 1950 to 1960. In addition, records of 148 patients were located in two London hospitals. At this time no data were available concerning the outcome of the 210 patients but follow-up data were being sought. Some concern was expressed about the study in relation to the nature of the underlying disease in the patients and the type of talcs used.

Presentation #10

Epidemiological Studies of Industrial Workers Exposed to Cosmetic Talc

The Boots Company in England are conducting two epidemiological studies on employees who had been exposed to talc; one is a morbidity

study and the other a mortality study. The morbidity study is being conducted by Dr. M. L. Newhouse, an epidemiologist who has worked extensively in the asbestos field. In this study all current workers are being evaluated for pulmonary function and symptoms of ill health in relation to the amount of talc dust to which they have been exposed. Some 22 men and 20 women subjects exposed to talc have been studied and the data obtained compared with 40 men and 40 women who were not exposed to talc dust. The talc dust concentrations to which the workers were exposed ranged from 1 to 3.5 mppcf but no data were available on the duration of the exposure. The data obtained to date reveal no difference in data obtained from the treated and control subjects, although Dr. Newhouse indicated that there was a trend in the reduction in pulmonary function in those exposed to the higher doses of talc dust.

The mortality study is being conducted by Dr. W. K. S. Moore, of The Boots Company. In this study the records of 3,000 ex-employees have been located and an attempt is being made to find the government records on these subjects that would give information concerning the cause of death of those who died. The incidence of the cause of death will be compared with that recorded for the U.K. population. At this time only 47 death certificates have been located, and these data were considered insufficient for analysis.

Discussion

A period of discussion took place at the end of the formal papers, with Professor Gareth Green being chairman of the discussion session. The objective of the discussion period was to summarize the data provided and determine what further studies would seem indicated.

The initial discussion centered around the composition and definition of cosmetic talcs. The biological role played by individual minerals in cosmetic talc dusts was discussed and it was suggested that further studies might be considered which would identify the biological activity of each mineral. It was pointed out, however, that talcs had fixed compositions and that evaluation of the total product in cells, animals and man should in fact give confirmation of the safety of the talcs and study of individual components would be of limited value or interest. It was mentioned that Italian grade talc represented a grade of talc with which other cosmetic grade talcs could be compared.

The animal studies were discussed and it was pointed out that the Battelle study was designed to assess cosmetic grade talc exposure encountered by the public and the doses used failed to reach an effect dose, while the MRC study was concerned with industrial exposure dosage and the dosage used did not show a no-effect dose. The desirability for a rat study showing a no-effect dose following chronic inhalation was suggested. A re-review of the dosages used in both animal and human studies was made which showed the very large multiples in dosage required to produce pathology in animals or man in relation to the talc exposure encountered by a baby.

Dr. Green concluded by saying that the data presented showed that there was no evidence to show that cosmetic use of cosmetic grade talc was a hazard to health and there was no disagreement with this statement from the group.

Dr. Gilson concluded the meeting by saying that cosmetic talc as used cosmetically was safe and, apart from a possible study to obtain a dose response in rats and possible biological study of contaminants in talc, there was no need for further studies to be conducted with cosmetic grade talc. He pointed out that it was important to disseminate the data presented at the meeting to others in the scientific community interested in them and recommended that the proceedings of the meeting be published in a scientific journal. He requested that reference samples of the Italian and Vermont talcs be made available to the MRC.

Commentary on the Meeting

The following points can be made about the meeting:

1. The data presented on cosmetic talc represent virtually all the data required for a new drug application on an ethical pharmaceutical product.

2. The data were presented to a group of experts in the field of dust diseases for review and discussion. Dr. J. C. Gilson, who is Director of the MRC Pneumoconiosis Unit, and his colleagues represent the official government specialists concerned with advising the British Government on health matters relating to dust environments.

3. Dr. Gilson was satisfied that the data presented showed cosmetic talc to be safe as normally used.

4. Dr. Gilson did not see any reason to do further studies, although Dr. Wagner expressed an interest in conducting a rat inhalation study to obtain a dose response, and Dr. Allison suggested that biological cell studies might be conducted with contaminants of talc.

5. Dr. Gilson is anxious to have the data provided published in the medical literature and will cooperate in developing a suitable manuscript for publication. The manuscript will not pre-empt any data presented at the meeting that have already been submitted for publication.

6. Representatives of the British Toilet Preparation Federation were well satisfied with the meeting and its outcome.

7. Dr. F. Roe, consultant to the TPF and tobacco industry, indicated his desire to write a position paper on talc for the TPF which could be published.

Suggested Future Action on Talc

As the result of the Cardiff meeting, the following action is recommended:

1. Type the proceedings from the tapes of the meeting. The typing of the proceedings will be done by J&J U.K.

2. Send a copy of the typed original proceedings of the meeting to Dr. Gilson for his review and further comment as to how he considers the discussion sections of the tapes should be edited prior to release of the edited proceedings to those who attended the meeting.

3. Discuss with Dr. Gilson the format of the manuscript to be submitted for publication in a medical journal and how the format is to be achieved.

4. Provide Dr. Roe with the proceedings of the meeting as well as Dr. Lord's manuscript and manuscripts developed by Dr. Hildick-Smith, to permit him to develop a position paper on talc. Dr. Roe's manuscript will be reviewed by J&J prior to release for the TPF.

5. Develop a manuscript on the safety factor data presented by Dr. Rolle and have the manuscript published in a medical journal.

6. No more studies on talc should be conducted at this time, as the meeting failed to identify the need for any further essential studies on talc.

7. Assemble available data on talc in a form which could be used by the OTC Panel if and when needed.

8. Consider which consultants might be available and could be used if needed for any open hearings that may occur in the OTC Panel review of talc.

9. Develop a nomenclature to clearly identify cosmetic grade talc from industrial grade talc for use in the market and in all publications.

10. Insure that if there are any cosmetic grade talcs on the market containing detectable amounts of asbestos that they are withdrawn from the market as soon as possible.

11. Consider provision of the edited proceedings of the Cardiff meeting to the FDA and OTC Panel.

Attachments

May 25, 1976

Gavin Hildick-Smith