RESEARCH ON ASBESTOSIS

Report on meeting held on Friday, 19th March, 1943, at the British Postgraduate Medical School.

Present:	Dr. W. H. Bateman (Chairman) Dr. T. H. Bolt. Dr. E. J. King. Dr. E.R.A. Merewether. Dr. W. Francis (Secretary)	Members of the Committee
	Sir Samuel Turner. Mr. R. G. Soothill.	Guests

In view of the fact that Dr. T. H. Bolt is expecting to join the Canadian Forces at the end of March, the time available was occupied mainly by a lecture and demonstrations by him on tissue culture technique, followed by a shorter dissertation on the animal experiments.

The histological examination of the sections of the rats' lungs used in the animal experiments has not yet been completed, but a large number of sections have been prepared and examined, and Dr. Bolt hopes to be able to complete this work before joining up and will then issue a tentative report on his findings for the whole of the work.

The first item on the agenda was a cinematograph picture describing tissue culture technique generally, with the addition of a number of slides made from photographs of the tissue cultures prepared by Dr. Bolt in his study of the effects of asbestos dusts on cell growth. The film had been prepared under the auspices of the Medical Research Council in connection with the study of cancer. It was very much appreciated by the visitors and helped Dr. Bolt considerably in his demonstration of the slides prepared during the work on the effects of asbestos on cell growth.

From the slides prepared during this work, it is evident that the presence of asbestos dust does not interfere unduly with the normal growth of the fixed cells. Whenever a small particle appears in the path of the advancing cell growth, the cells develop in the normal manner and the particle becomes engulfed in a fixed cell or, if the particle is too large to be contained in a single cell, the cells divide and rejoin after the obstruction. A number of small particles were seen completely surrounded by fixed cells and some also were surrounded by mobile cells.

Dr. Bolt observed that the presence of the fibre in the fixed cells appeared to have no effect at all upon the tissue, but he considered that the presence of a particle of short fibre in a mobile cell would reduce its motivity.

Dr. Bolt also stated that some evidence had been obtained that the rate of solution of asbestos in the tissue culture medium was apparently greater than the rate of solution in a similar fluid in the absence of the living tissue though, at a later stage in the proceedings, it was agreed that the evidence was not positive on this point.

A number of slides illustrating sections of the rats' lungs were shown immediately following the film, and these, in general, appeared to confirm the findings of the tissue culture work in that there was little or no evidence of cell destruction or poisoning due to the presence of the asbestos, either in the case of the longer fibres or

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in the case of the shorter fibres. On the other hand, it was quite clear that the fibres tended to congregate in certain portions of the lungs, causing obstruction of the air passages, and, frequently, scar tissue was present beyond these obstructions, resulting from the incidence of patchy pneumonia.

No asbestosis bodies were observed in these slides, and this agrees with a recent statement by Dr. Gardner that asbestosis bodies are not produced in the lungs of rats into which asbestos fibre has been injected. Indeed, the general opinion seems to be that the main effect of the presence of asbestos in the lungs of the rats is to cause obstruction of the breathing passages, reducing the effective lung area and making it easier for the development of pneumonia or other pulmonary diseases. Obviously, in this case, the longer fibres are the more dangerous, since the small fibres, below about 5μ in length, do not normally obstruct the lung passages except when a large number of these congregate together. Such small particles of asbestos can readily be surrounded by phagocytes and these may therefore sometimes be removed from the lungs in the normal manner, though, as mentioned earlier, the motivity of such cells is greatly reduced when they contain asbestos.

At this stage the party adjourned to the laboratories to see the apparatus now in use for tissue culture work, and particularly the set-up by Dr. Bolt to obtain a film showing the effects of asbestos dust on the growth of tissue from chicken or human embryo. Unfortunately, Dr. Bolt had to leave early, but before leaving he summarised the position of the animal experiments and answered a number of questions relating to the tissue culture work and to the animal experiments.

The following is a brief summary of the animal position on 19th March, 1943:-

Experiments 17 - 22 17 animals out of an original 68 were still alive after 322 days. In this experiment, alumina "A" was introduced into the lungs of the animals in addition to asbestos.

In experiments 23 - 27, using 15μ fibre, 21 out of 37 rats were still alive after approximately 240 days.

In experiment 26 factory dust screened through a 300 mesh sieve was used and 3 animals out of 12 were still alive after 239 days.

In experiment 28 loom dust sieved through a 300 mesh sieve was used. 3 out of 12 animals were still alive after 159 days, whilst in experiment 29, using C. & G. asbestos fibre of length 7½μ, 2 out of 12 animals were still alive after 155 days.

All the animals used in the experiments 1 - 12 are now dead; the longest survival with short asbestos fibre being 329 days and the longest survival with the 15μ asbestos being 189 days. In these experiments excessive doses of fibre were introduced into the lungs, and mortality during the operation and immediately following was high. Consequently, the only conclusion to be drawn from these experiments is that the short fibres are less harmful than the longer fibres. The final conclusions from experiments 17 - 29 must await histological examination of the lungs after death, but there does appear to be some slight indication from experiments 17 - 22 that the presence of alumina "A" is beneficial.

Dr. Merewether gave a brief account of his discussions with Dr. Gardner of the Saranac Laboratories, and also gave some information regarding the effect on the life of the workers in the Canadian mines of introducing small quantities of powdered aluminium into the air intake.

With regard to the work done by Gardner, Dr. Merewether said that much of the earlier work was confirmed using purified asbestos dusts instead of the impure dusts used in the early experiments. He also stated that Dr. Gardner had found that the formation of asbestosis bodies apparently does not occur in the lungs of rats; but he had been able to detect the formation of these bodies in the lungs of guinea pigs.

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With regard to the effect of aluminium in small concentrations in the air on the health of the workers in some of the Canadian mines, Dr. Merewether said that this was encouraging, and there is every hope that the procedure will be effective in greatly reducing the incidence of silicosis in these mines.

It will be recalled that at the outset of our experimental work on asbestosis it was hoped that several doubtful points of Gardner's work would be decided and it may be useful here to repeat these questions, and indicate to what extent answers have been obtained.

1. Is long fibre more harmful than short?

All the evidence seems to indicate that fibre of length greater than about 5μ is more harmful than fibre below 5μ in length.

2. Do the different types of asbestos behave differently?

No indication has been obtained that one fibre is more dangerous than another.

3. Does the presence of small quantities of alumina or aluminium powder suppress the solubility of asbestos in the body fluids in vitro?

The answer is that certain types of alumina do reduce the solubility of asbestos and that aluminium powder is even more effective.

4. Does the addition of alumina increase the life of the animals?

The answer here is indefinite, though there is some slight indication that the presence of one type of alumina is beneficial.

5. Is asbestos toxic to living tissue?

The work has shown that asbestos is definitely not a cell poison in the ordinary sense.

It was agreed that the results were sufficiently promising to warrant the continuation of the animal experiments to complete the life cycles of the animals already innoculated and to commence a further experiment on the addition of aluminium to the animals in order to answer more positively question no.4, particularly in view of the horrible effect of the use of aluminium in reducing silicosis in mine workers.

In view of Gardner's observations on the differences between guinea pigs and rats, it was further decided to use guinea pigs for this additional series of experiments.

The programme outlined is to innoculate 24 guinea pigs with pure asbestos fibre of 5μ length and to innoculate a further 24 guinea pigs with some of the same sample of asbestos with the addition of a small quantity of the powdered aluminium used by Irvin in the Canadian mines. Dr. King has a sample of this aluminium and has expressed his willingness to supervise these experiments with the assistance of junior help on the school staff.

Dr. Belt will write a preliminary report on the results of the tissue culture and animal experiments, and Dr. Irvin-Brown will round off the remaining work required to be done on the tissue culture experiments

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ITEMS FROM RESEARCH DEPARTMENT

ASBESTOSIS RESEARCH

On Friday, March 19th, a meeting was held at the British Postgraduate Medical School of the Asbestosis Committee to discuss the state of the asbestosis research work being carried out for us by Drs. E. J. King and T. H. Belt.

The following members of the Committee were present:-

Dr. W. H. Bateman (chairman)
Dr. T. H. Belt
Dr. E. J. King
Dr. E. R. A. Merewether
Dr. W. Francis (secretary)

Sir Samuel Turner and Mr. R. G. Soothill were also present as guests.

It will be recalled that Dr. T. H. Belt is expecting to join the Canadian Forces at the end of March, and has been working intensively on our behalf during the last two months in an endeavour to complete the tissue culture work and to derive some positive conclusions from the animal experiments before leaving. Consequently the time available was occupied mainly by a lecture and demonstrations by Dr. Belt on tissue culture technique, followed by a shorter dissertation on the animal experiments.

The histological examination of the sections of the rats' lungs used in the animal experiments has not yet been completed, but a large number of sections have been prepared and examined, and Dr. Belt hopes to be able to complete this work before joining up and will then issue a tentative report on his findings for the whole of the work, so that we will be in a position to act upon any findings that appear to have any practical significance in connection with the incidence of asbestosis in the factory. Since it is unlikely that this report will be available for the Board Meeting on April 1st, I am attempting to anticipate these findings for the benefit of the Board, and if this anticipation should prove wrong in any material instance, I will prepare an additional statement of correction for the next Board Meeting.

The first item on the agenda at the meeting was a cinematograph picture describing tissue culture technique generally, with the addition of a number of slides made from photographs of the tissue cultures prepared by Dr. Belt in his study of the effects of asbestos dusts on cell growth. The film had been prepared under the auspices of the Medical Research Council in connection with the study of cancer.

The first section showed the normal development of lung tissue allowed to grow in a favourable medium on a cavity slide at a controlled temperature. In this picture the gradual growth of the cells towards the circumference of the cavity from a small central scrap of tissue was well illustrated, and