"(c) the Medical Research Council on all medical research in or for tropical or subtropical countries financed from their own budget."

The operations of the Medical Research Council are not territorially limited, and for that reason these proposals should provide security of tenure of appointment for those already in the Overseas Research Service of the British Government who are serving in territories soon to be granted independence. They should also provide an attractive career structure for new recruits to medical research overseas. The Medical Research Council proposes to offer to young workers interested in medical problems overseas initial appointments for five years, the first three of which will be spent abroad with the possibility of renewal at the end of this period. If, however, the worker finds tropical work not to his liking he will spend the remainder of the first appointment in a home department allied to his interests. Where research of value is hampered by inability of a newly independent territory to find funds hitherto provided by the Colonial Development and Welfare Act, it should also prove possible for the Medical Research Council with its non-territorially restricted budget to ensure continuity. The proposals will command wide support both at home and overseas, and those concerned with their formulation are to be congratulated on their foresight.

INFECTED COCONUT

An outbreak of typhoid fever and salmonella infection occurring in Australia in 1953 was traced to desiccated coconut contaminated with various organisms of the salmonella group.[1] Numerous strains of salmonella were isolated from the coconut, among them *Salmonella senftenberg, S. orion,* and *S. potsdam,* which were the organisms most frequently isolated from infected cases and symptomless excretors. It was only after some time that *S. typhi* was isolated from one sample of the incriminated brand of coconut. This strain was of the same phage type as those isolated from patients in the epidemic who were suffering from typhoid fever. It is perhaps worth remarking that *S. typhi* of this phage type, E.1, was at that time endemic in Australia. All the coconut found to be contaminated had been imported from Papua. Samples of Sinhalese coconut which were cultured during the investigations were free from salmonellae, though they were found to contain a number of coli-aerogenes and paracolon strains. N. Kovacs[2] isolated *S. senftenberg* from 30 and *S. nyborg* from 7 samples of Papuan coconut which he examined during the outbreak, and subsequently isolated salmonellae in 9 out of 35 samples of Sinhalese coconut. One of these samples contained *S. paratyphi-B*; 2 contained a new serotype, *S. perth*; and 5 contained *S. butantan*; only one sample was contaminated with more than one strain, and this contained *S. edinburgh* and *S. perth.*

Between July, 1959, and March, 1960, 851 samples of desiccated coconut imported into Great Britain from Ceylon were tested by members of the Public Health Laboratory Service,[3] and 76 samples were found to contain salmonellae. *S. paratyphi-B, S. senftenberg,* and *S. bareilly* were the commonest types isolated. The proportion of samples found to be contaminated varied according to the grade of the material examined. All samples of chippings and flakes which were examined were negative. The highest proportion of contaminated samples was from coconut flour, which was milled in Britain from fine coconut. The authors suggest that the higher proportion of positive samples in flour was probably due to the greater mixing which the material received during processing, leading to a more even distribution of organisms. They could find no evidence that further contamination occurred during milling, though they do not seem to have substantiated this experimentally. There was little difference in the proportion of contaminated samples from bakehouses, docks, or from consignments packed in cases or in paper sacks. The authors concluded from this that it was unlikely that the coconut was contamined after packing in Ceylon. Total bacterial counts at 37° C. were all less than 50,000 per gramme. *Escherichia coli* and "non-faecal" types of coliform bacilli were found in some samples.

There are many opportunities for contamination with organisms of the salmonella group at all stages of manufacture of desiccated coconut. Without going into details of the manufacturing process, it is enough to say that the material is exposed to faecal contamination from humans; animals, including rodents and birds; and from organic and farmyard manures. There is some evidence that the nuts themselves may be permeable to micro-organisms.

It has been shown experimentally that salmonellae grow well on moist coconut flesh in warmth. Although coconut meal is desiccated for about 25 minutes at a temperature of 180°–210° F. (82–99° C.) it has been shown that *E. coli* survived the drying process when the desiccation temperature was 180° F. (82° C.) or more for 40 minutes,[1] and, while the process of desiccation must reduce the number of organisms, it is clear that desiccation alone is insufficient to sterilize the material effectively. Various methods of treating coconut are being tried, including heating to 130° F. (54° C.) for 9 or 10 days; heating to a high temperature for a short time; steam-heating and the use of boiling water; disinfection with ethylene oxide gas; and gamma irradiation.

The numbers of salmonellae present in coconut are so low that infection is likely to occur only when contaminated coconut is in contact with foods which would encourage the multiplication of the organisms under warm, moist conditions, or when large amounts of raw coconut are eaten. When coconut is incorporated in cooked confections it may contaminate other

[1] Wilson, M. M., and Mackenzie, E. F., *J. appl. Bact.*, 1955, **18**, 510.
[2] Kovacs, N., *Med. J. Aust.*, 1959, **1**, 557.
[3] Galbraith, N. S., Hobbs, B. C., Smith, M. E., and Tomlinson, A. J. H., *Monthly Bull. Minist. Hlth Lab. Serv.*, 1960, **19**, 99.

foodstuffs in the kitchen or bakery either directly or by means of utensils or on the hands of food-handlers.

At present port health authorities in Britain sample 5% of imported batches, and if positive results are obtained a further 10% are tested. If positives are found at the second sampling, the contaminated batches are condemned. But, as is the case with so many other imported foodstuffs which are subjected to bacteriological control, the organisms are so unevenly distributed throughout the material that their presence may be missed in samples which are of necessity quantitatively small in relation to the amount in the container being sampled. Production of a bacteriologically safe coconut must depend on improvement in the hygienic conditions in the plantations and factories in the country of origin, and in the tracing and elimination of the sources of contamination, all of which may be a slow process. Alternatively, a suitable disinfecting or sterilizing procedure must be developed which would be applicable on a large scale to the finished product without damaging it or impairing the qualities which make it desirable as an ingredient of puddings, cakes, and confectionery.

AMPHETAMINE OVERDOSAGE IN AN ATHLETE

The increase in body temperature after exercise is entirely physiological and, in general, is no cause for alarm. But sometimes if body cooling is obstructed by clothing, or climatic conditions are unexpectedly severe, heat exhaustion may be induced by exercise, or even heat stroke may develop with a fatal outcome. Football, boxing, and cross-country running have all seen casualties of this type. Now J. Bernheim and J. N. Cox[1] report upon such a case in bicycle racing. Towards the end of a gruelling 119-mile (191 km.) race, which included 7,475 ft. (2,300 m.) of ups and downs, one of the tail, an experienced 25-year-old amateur, was seen to be in difficulties: he collapsed and was immediately taken to hospital. On admission his rectal temperature was 109.4° F. (43° C.), his pulse-rate 140, and his blood-pressure 90/51 mm. Hg. Despite vigorous treatment, including ice packs, he died about five hours later. The body temperature at death is not reported, so the success of the cooling measures cannot be assessed. The immediate cause of death was cardiovascular collapse. At post-mortem examination little abnormal was found except for a hypertrophied heart, minor renal and suprarenal changes, and numerous subseral and submucosal haemorrhages in the viscera, and petechial haemorrhages in the brain.

The picture in this case resembled that described by N. Malamud, W. Haymaker, and R. P. Custer[2] in their report on heat stroke in the U.S. Army, and but for two things one might have accepted this as another example of a man's temperature going too high and reaching the point at which sweating fails.[3] First there are the climatic conditions; although described as "stifling," these were not unduly severe—the temperature was 78.8° F. (25.9° C.) and the relative humidity 56%—especially as cyclists provide their own air movement. No description is given of how this patient was clothed, but no one else in the race is reported to have suffered from the heat. The second discordant note is that the patient's skin on admission was not hot and dry, as is always the case in heat stroke, but of "normal humidity." There was in fact another possible cause of death, amphetamine poisoning. During the race this man had taken 105 mg. of amphetamine, partly in coffee and partly as tablets. Less than 1 mg. was recovered unabsorbed from his stomach.

The authors point out that, although 105 mg. is well below the usually acepted lethal dose of amphetamine, deaths have been recorded after such doses, and the post-mortem findings were as compatible with an overdose of this drug as with heat stroke. They conclude that death resulted from the combination of severe exercise, heat, and amphetamine overdosage. Were it not for the extraordinarily high rectal temperature reported this man's death might have been attributed almost entirely to amphetamine in spite of the size of the dose: certainly the circulatory collapse was probably as much due to the drug as to the heat. Concern about the use of amphetamine by athletes[4] has recently been expressed in the U.S.A. As Professor J. H. Gaddum[5] has written, it induces "a mood of cheerful confidence," which, as in the case of the racing cyclist, may "lead to trouble."

IMMUNOLOGICAL REACTIONS IN SILICOSIS

The capacity of silica to produce collagenous fibrosis in the tissues of man and of many other animal species is still a perplexing problem. The forms of silica capable of doing this are varieties of silicon dioxide often called free silica. In human pathology quartz is the form which is of greatest importance. Other forms of free silica are tridymite, cristobalite, and vitreous silica, which differ from one another slightly in their atomic patterns[1] but they all are chemically 100% silicon dioxide. These four different forms of free silica have considerably different fibrogenic activity. For more than 30 years it had been thought that silicosis was due to the silica going into solution in the tissues, and that the differences in fibrogenicity were related to differences in solubility. This is not so, since the four forms of free silica have equal solubilities, and another explanation must be sought to account for their different fibrogenic capacities.

It is evident that the surface structure of silica particles is important because alteration of it by coating with iron or with aluminium can depress the fibrogenicity. On the other hand, if the outer and more soluble layer of the particles is removed by etching, then the fibrogenicity of the remaining portion of the

[1] Bernheim, J., and Cox, J. N., *Schweiz. med. Wschr.*, 1960, **90**, 322.
[2] Malamud, N., Haymaker, W., and Custer, R. P., *Milit. Surg.*, 1946, **99**, 397.
[3] Ladell, W. S. S., *Trans. roy. Soc. trop. Med. Hyg.*, 1957, **51**, 189.
[4] See annotation, *Brit. med. J.*, 1959, **2**, 1464.
[5] Gaddum, J. H., *Pharmacology*, 1959, Oxford University Press, London, p. 222.

particles is increased although the solubility is reduced. In order to produce its pathogenic effects it seems that quartz must first be taken up by macrophages, and there is clear evidence, as for instance from the work of J. Marks and D. M. James,[2] that quartz depresses the metabolism of these cells and many of the injured cells die. P. F. Holt[3] believes that within the cytoplasm of the phagocytes a collagen precursor is formed which concentrates, polymerizes, and reacts with mono-silicic acid as it is freed from the quartz surface, with the result that pro-collagen is changed into collagen. This is a modified solubility theory.

Other workers, however, have been attracted to a completely different view of silicosis, and regard it as an immunological process. This was first suggested by I. Webster[4] (1954). A good summary of the present position is given by E. C. Vigliani and B. Pernis,[5] and was discussed at the meeting of the Association of Clinical Pathologists last April.[6] Pernis and L. Pecchiai[7] showed that silicotic nodules contain 60% globulins including β- and γ-globulins. These occur as amorphous material in silicotic nodules. Electron microscopy shows collagen fibres embedded in the amorphous substance, the structure thus differing from simple scar tissue. H. Antweiler and E. Hirsch[8] found that quartz coated with homologous serum albumin causes antibodies to form when it is injected into laboratory animals. These antibodies can be detected by agglutination tests. Injected quartz acts as an adjuvant to the formation of antibodies in unrelated immunological reactions—for example, the resistance to typhi-murium infection is increased in mice previously injected with tridymite.[9] The relationship of an unrelated immunological reaction to silicosis was studied by D. E. B. Powell and J. Gough,[10] who showed that the immunization of rabbits with horse serum resulted in subsequent silicotic lesions being larger and more clearly demarcated and more collagenous. The production of anti-egg-albumin in rabbits previously injected with tridymite was five to six times higher than in control rabbits.[11] These observations are pertinent to the observation of A. Caplan[12] that in miners with rheumatic disease the lung lesions are radiologically different from those in miners without arthritic joints. Gough and his colleagues[13] identified a corresponding difference in the pathology of the lesions, showing that pneumoconiosis renders the lung vulnerable to the nodular rheumatoid process. This may be an adjuvant immunological effect. We are left with the question whether silicosis is a specific immunological process or whether the silica merely acts as an adjuvant in other antigen–antibody reactions, and an obvious question is whether the special liability of the silicotic man to develop tuberculosis is in some way concerned with alteration in immunology or in sensitivity to that disease.

[1] Nagelschmidt, G., in *Industrial Pulmonary Diseases*, 1960, edited by E. J. King and C. M. Fletcher, London.
[2] Marks, J., and James, D. M., *J. Path. Bact.*, 1959, **77**, 401.
[3] Holt, P. F., *Pneumoconiosis*, 1957, London.
[4] Webster, I., *Proc. Transv. Mine med. Offrs' Ass.*, 1954, **34**, No. 349.
[5] Vigliani, E. C., and Pernis, B., *J. occup. Med.*, 1959, **1**, 319.
[6] *J. clin. Path.*, 1960, **13**, 271.
[7] Pernis, B., and Pecchiai, L., *Med. d. Lavoro*, 1954, **45**, 205.
[8] Antweiler, H., and Hirsch, E., *Z. Immun.-Forsch.*, 1957, **114**, 378.
[9] Pernis, B., and Bolis, L., *Proceedings of the Third International Symposium of Reticulo-endothelial Society*, Rapallo, in press.
[10] Powell, D. E. B., and Gough, J., *Brit. J. exp. Path.*, 1959, **40**, 40.
[11] Ghiringhelli, L., and Pernis, B., *Med. d. Lavoro*, 1958, **49**, 665.
[12] Caplan, A., *Thorax*, 1953, **8**, 29.
[13] Gough, J., Rivers, D., and Seal, R. M. E., ibid., 1955, **10**, 9.

OPHTHALMIC HOSPITAL OF THE ORDER OF ST. JOHN

The new ophthalmic hospital which the Order of St. John has built in Jerusalem is now complete, and a photograph of the building appears in this issue (p. 614). Containing seventy beds and a large out-patient department and incorporating a research institute and training school, the hospital is the most up to date and important ophthalmic centre in the Middle East. It will be opened on October 11 by King Hussein of Jordan in the presence of the Duke of Gloucester, Grand Prior of the Order.

The hospital has a long and eventful history, going back to A.D. 600, when the first hospital was founded to care for the Christian pilgrims to the Holy Sepulchre. When the Holy Land was lost, the Order of St. John moved the hospital first to Cyprus, then to Rhodes, and finally to Malta. After 700 years, in 1882, the Order once again established a hospital in Jerusalem, this time for eye diseases. During the second world war the hospital did invaluable work for the Services and the civilian population, but no sooner had some necessary rebuilding been undertaken than fighting broke out between the Arabs and Israelis, and once again, in 1948, the hospital had to be abandoned. Since then the work has been continued in temporary premises.

The completion of the new building owes much to Sir Stewart Duke-Elder, F.R.S., the Hospitaller of the Order. Five years ago, after exploring the possibilities of co-ordinating ophthalmic work throughout the Middle East, he selected a site, and with the help of governments and industrialists plans were quickly put in hand for the building of the new research institute and the hospital. The former was completed in 1956 and is staffed by a team of workers under the auspices of the Medical Research Council. The two corner-stones of the main building were laid eighteen months ago—one by the Chancellor of the Order, Lieutenant-General Sir Henry Pownall, and one by the Hospitaller, Sir Stewart Duke-Elder—and now the project is complete. The cost so far has been £325,000, and the hospital will need continuing financial support in the future. The importance of its work can hardly be exaggerated, for now that the trachoma virus has been isolated there are hopes that this disease, which is particularly devastating in the Middle East, will be brought under control. The new hospital and research institute in Jerusalem will be one of the spearheads in the final attack against this disease.