cytochromes b, a and a_3 on the inner side and cytochromes c and c_1 on the outer side of the cristal membrane, with cytochrome c_1 oxidizing dihydroubiquinone and releasing protons outwards.

Several speakers attempted to relate their observations on isolated mitochondria to the situation *in vivo*. One of the most challenging problems in the relation of the mitochondria to the other cell components is the coordination of the mitochondrial and the nuclear genetic systems. Dr G. Schatz (Ithaca) showed that the mitochondria of anaerobically grown baker's yeast (promitochondria) possess cristae, but lack a respiratory chain. The promitochondria possess a functional system for synthesizing protein, which incorporates amino-acids into the inner membrane, some of it into OSCP. When the cells are exposed to oxygen the promitochondria rapidly form a respiratory chain. These findings are consistent with the possibility that oxygen derepresses some cistrons on mitochondrial DNA.

MINERAL METABOLISM

Phosphonates to protect Bone

from our Medical Biochemistry Correspondent

COMPOUNDS have been found that may be useful drugs for treating disorders of mineral metabolism. Pyrophosphate, which is thought to play a part in regulating mineral metabolism—the deposition of calcium phosphate to form bones and teeth—is broken down by pyrophosphatases and rendered inactive in some tissues. Recent work has suggested, however, that diphosphonates have very similar effects but are not susceptible to enzyme hydrolysis, which might make them useful drugs.

Fleisch, Russell and Francis (*Science*, **165**, 1262; 1969) found that the release of calcium and phosphate ions from crystals of hydroxyapatite, which are found in bones and teeth, was inhibited by a solution of pyrophosphate or two diphosphonates (sodium dichloromethylenediphosphonate and sodium methylenediphosphonate), but not by the monophosphonate. Cultured foetal skull bones of mice lost minerals when parathyroid extract was added, but this resorption could be inhibited by both diphosphonates and pyrophosphate, although not by the monophosphate.

Diphosphonates were also active against bone resorption *in vivo*. Thyroids and parathyroids were removed from male rats, and four days later blood samples were taken before, and six hours after, the injection of parathyroid extract. The increase in plasma calcium after this treatment was abolished if the rats had previously been treated with a diphosphonate. Treatment with dichloromethylenediphosphonate also reversed the high concentration of calcium in the blood induced by parathyroid extract. This suggests that the diphosphonates could be useful agents for treating other conditions in which bony tissue is lost, such as osteoporosis, which is extremely common in elderly women.

Diphosphonates may also prevent calcification in soft tissues. Fleisch *et al.* also showed that, like pyrophosphate, the diphosphonates do not affect the precipitation of amorphous calcium phosphate but inhibit the growth of hydroxyapatite crystals (*Science*, **165**, 1264; 1969). The compounds also increase the minimum product ($Ca \times PO_4$) required for the precipitation of calcium phosphate. A monophosphonate that was tested also increased the concentration required for precipitation but had no effect on crystal formation.

Fleisch *et al.* also found that diphosphonates could inhibit calcification in soft tissues *in vivo*. Rats given excess vitamin D_3 developed aortic and renal calcification, which was inhibited if they were given diphosphonates orally or subcutaneously. The most interesting aspect of this work is that, whereas pyrophosphate inhibits aortic calcification only, the diphosphonates also reverse the effects of excess vitamin D in the kidney. This is almost certainly a consequence of the resistance of the diphosphonates to attack by kidney pyrophosphatase. If the compounds are safe enough for clinical use, they may therefore be valuable in treating several disorders of mineral metabolism.

CANCER

Bacteria as a Cause

from a Correspondent

THE meeting of the New York Academy of Sciences, held from November 5 to 8, to discuss unusual isolates from clinical material, covered some rarely discussed topics. The theme was the possible pathogenic roles of various bacteria, L-forms, mycoplasmas and so on not usually regarded as harmful, and there was a short symposium on bacteria in relation to cancer.

The realization that tumour viruses cannot be ignored in relation to human disease seems to have allowed some relaxation of the attitude that bacteria should not be discussed as a possible cause of cancer.

Dr S. Inoue (Gunma University, Japan) and Dr M. Singer (Case Western Reserve University) discussed further experimental evidence for their earlier work, which produced the first indubitable example of an experimentally induced bacterial tumour (*Nature*, **205**, 408; 1965). The organism concerned, which has proved to be a mycobacterium, has recently been used to induce tumours after injection into other species of amphibia, including *Xenopus*. This news gave support to the claim by Dr E. Alexander-Jackson (University of California, San Diego) that the Rous sarcoma virus is the mycoplasma-like L-form of a similar, pleomorphic, variably acid-fast bacterium.

There is good evidence that such bacteria are associated with human tumours, and in mice the extent of infection can be shown to be numerically coordinated with the incidence of tumours. Dr P. Pease (University of Birmingham, England), who believes that the bacteria belong to the *Listeria/Erysipelothrix* group and are widely distributed in healthy persons and animals (*Nature*, **215**, 936; 1967), pointed out that this type of distribution is characteristic of tumour viruses in susceptible populations, and that the bacteria themselves have distinct resemblances to the tumour bacteria of plants.

The general feeling at the symposium was that if not everybody accepted the more enthusiastic ideas of a direct and uncomplicated relationship between cancer and bacteria, at least the problem does exist and deserves more work and consideration than it has received. The classical lines of cancer research cannot claim such success that their protagonists may reasonably dismiss out of hand all analogy with a phenomenon that is observable in both plants and lower vertebrates.