refined practice, and often draws, as here, on specialized procedures, such as double-resonance experiments to allocate each peak in the spectrum. With the restriction, derived from X-ray crystallography, of a two-fold symmetry axis in the molecule, the requirement, deduced from proton coupling constants, for certain fixed dihedral angles, and the need to match a number of chemical shifts by reasonable internal interactions, a model of the structure has been derived with some confidence. The molecule is essentially flat, and four internal hydrogen bonds are defined.

CARDIOVASCULAR DISEASE

Heart Death Hazards

from our Medical Biochemistry Correspondent

FOR some time most research on cardiovascular disease has been concentrated on the role of lipids. The recent MRC trial, however (*Nature*, **220**, 15; 1968), showed no difference in the death rate or number of heart attacks between a group on a diet rich in polyunsaturated fatty acids and a control group.

In the search for other factors, it has been suggested that water hardness affects the incidence of cardiovascular disease, although other workers have been unable to find a significant effect. Earlier this year, Crawford, Gardner and Morris (*Lancet*, i, 827; 1968) showed that there is a significantly greater death rate from cardiovascular diseases in areas which have soft water. They compared death rates at ages between 45 and 74 with hardness of water for the 61 county boroughs with populations greater than 80,000 (at the 1961 census). Death rates from most causes showed a slight (just significant) negative correlation with water hardness; the death rate from bronchitis (often associated with cardiovascular disease) was even more significantly affected, with a product moment correlation coefficient of $-0{\cdot}40$ to $-0{\cdot}45$; for cardiovascular disease the association was even greater, with a product moment correlation coefficient of $-0{\cdot}60$ to $-0{\cdot}70$. The cardiovascular death rate was related to Ca^{++} concentration more than to the concentration of any other ion. Differences in latitude also appeared to affect the death rate from cardiovascular disease, but had less effect than water calcium. Poor social conditions affect the death rates from bronchitis and "other causes" but not the death rate from cardiovascular disease.

Even more interesting is the more recent demonstration that carbon disulphide in the air seems to increase the incidence of cardiovascular diseases. Only one other investigation has revealed an occupational factor in coronary heart disease, partly because there are so many deaths from this cause in the general population. Tiller, Schilling and Morris (*Brit. Med. J.*, **4**, 407; 1968) found that the proportion of deaths due to heart disease was 42 per cent in viscose rayon process workers, 24 per cent in other workers in rayon factories, 17 per cent in a group of local controls and 14 per cent in the country as a whole. This significant difference might simply have meant that rayon workers were protected from other causes of death and more likely to die of heart disease. For one factory, however, it was possible to calculate death rates per 1,000 man-years, and this showed that workers in the spinning department had more than twice the expected numbers of deaths from heart disease. Nearly half the measurements of carbon disulphide in the spinning room had approached the limit accepted at present. The men had experienced some exposure to hydrogen disulphide, but this was much less than the carbon disulphide exposure. Carbon disulphide is also released during the making of viscose rayon, but hydrogen disulphide is not. Viscose makers in the most modern factory had six heart deaths instead of the five expected, while in two older, less well ventilated factories there were thirteen deaths instead of the 4·6 expected. This seems to establish carbon disulphide as the villain of the piece.

If exposure to low concentrations of carbon disulphide can increase the risk of heart disease, the increasing quantities of other sulphur compounds in the atmosphere are bound to become a cause for concern. An investigation of the effects of carbon disulphide might at the least be a much needed stimulus to the biochemical study of cardiovascular disease.

BIOCHEMISTRY

Proteolytic Enzymes

from a Correspondent

A MEETING on proteolytic enzymes at the Royal Society last week formed a valuable synthesis of the considerable body of evidence which has been obtained from crystallographic, biochemical and organic chemical techniques. The meeting opened with an account by Dr D. M. Blow (Cambridge) of the more precise redetermination of the structure of α-chymotrypsin. This had led to the exciting discovery of a new buried acid group, Asp-102, following the re-examination of the sequence of the residues in this region by Dr B. S. Hartley (Cambridge). The unfavourable situation of this buried charged group is alleviated by transfer of the negative charge to the surface of the enzyme by hydrogen bonding through a histidine, His-57, to Ser-194. The transfer of the charge to the serine allows it to act as a powerful nucleophile in the hydrolysis action, a mechanism which is likely to be of general relevance to other serine proteinases, as the X-ray studies on elastase by Dr H. C. Watson and Mr D. M. Shotton (Bristol) have shown. Their model, constructed from a 3·5 Å electron density map, had been completed at the beginning of the week after only one man-year of work on this protein. It is very similar to the structure of chymotrypsin, including the same charge relay system for the activation of the serine and a charge–charge interaction between the acid residue adjacent to the serine and the α-amino group, which contributes to the stabilization of these enzymes in the active conformation. Dr B. S. Hartley's paper showed how the homologies in sequence of the serine proteinases may help to elucidate the mechanism of blood clotting since the *B* chain of thrombin has a sequence much like that of chymotrypsin.

The primary sequence of the bacterial serine proteinase, subtilisin BPN′, is completely different from that of the mammalian enzymes. Thus the paper by Professor J. Kraut (University of California) on the structure of subtilisin at 2·5 Å resolution caused considerable interest, because he revealed that the mechanism of activation of the serine remains the same in this enzyme although the tertiary structure is completely different from chymotrypsin and elastase, and