This final chapter is not intended to provide a comprehensive overview of the topics discussed previously. Instead it will highlight those topics for which a better understanding is essential before the significance of zinc for human health and wellbeing can be fully assessed. It will also consider some troublesome controversies.

The Functional Roles of Zinc

As with other trace elements and micronutrients, discovery of the essentiality of zinc was followed by an extensive series of accounts of studies of purified enzymes for which either intrinsic zinc plays a functional role or extrinsic zinc modifies activity.

The list of more than 200 enzymes now known to contain zinc is impressive and, as indicated in Chap. 2, the range of their functions is extensive (Hambidge et al. 1986). However, the most notable feature of our newer biochemical understanding of the roles of zinc is not so much the variety of its functions as an essential catalytic component of such enzymes but rather its role as a structural constituent of enzymic and non-enzymic proteins and probably of polynucleotides. Zinc appears either to confer structural and metabolic stability or govern the tertiary architecture and thus the biological function of a wide range of macromolecules. The first suspicions of such an organizational, as well as a catalytic, role for zinc, emerged from investigations of the functions...
of zinc in alcohol dehydrogenase, within which enzyme it is possible to
differentiate zinc associated with the functional, catalytically active centre from
the zinc, less firmly bound, which stabilizes the polymeric structure of the
enzyme. Such an organizational role is apparent for a growing range of other
proteins (see Morisawa and Mohri 1972; Hesketh 1981; Williams 1984). Typical
of the diversity of such roles is evidence that differences in zinc status of the
donor tissue markedly influence the in vitro stability of α-mannosidase, and
the more recent finding that zinc determines receptor-site structure of the
enzyme transcriptase factor IIIA (as considered in Chaps. 2, 5 and 7). It will
be surprising if evidence for such structural roles does not increase substantially
in the near future.

The tacit neglect of the major proportion of body zinc associated with tissue
proteins that relegates it virtually to the category of a trivial adventitious
contaminant is inconsistent with the behaviour of the element at times when
growth rates change or tissue integrity is prejudiced. Thus, it is well established
that tissue catabolism provoked for example by protein/energy deficiency or
calcium deficiency can be the stimulus to release of sufficient zinc to ameliorate
or preclude development of pathological responses to a low zinc intake (Masters
et al. 1986). Conversely, the anabolic response to nutritional rehabilitation or
following tissue injury not only depletes the plasma pool of zinc but frequently
provokes the first appearance of clinical signs of deficiency. The complexity
of equilibria governing such relationships is evident from the initial response
to zinc repletion of the severely deficient infant (as described for example by
Golden and Golden 1981). The resumption of growth following zinc therapy
can be accompanied, paradoxically, by a fall in circulating plasma zinc.
Consistent and significant decreases in plasma zinc have also been noted
recently when zinc-depleted mature subjects showing no clinical signs were
first returned to diets normal in zinc content (C. Bosworth, personal communi­
cation). Such observations are incompatible with any concept that zinc is
merely an exchangeable, mobile constituent of the increment of new tissue
synthesized in response to an improved zinc status. More likely, zinc stimulates
protein synthesis – perhaps indirectly – while also modifying tertiary protein
structure in a way which promotes more complete exposure of zinc-binding
ligands in association with which the element serves its structural role(s).

If zinc has such extensive structural roles rather than being present merely
as a “pollutant” of the mass of body protein, it is to be expected that a decline
in body zinc status might be accompanied by an acceleration of protein
turnover. Many studies have been made of the effects of zinc deficiency on
protein synthesis; of these, many have given equivocal results and few have
been accompanied by corresponding studies of protein degradation rate. Thus,
in the context of our suggestion that zinc may have a stabilizing role it is
notable that among the very few studies of effects of zinc deficiency on protein
turnover, one with rats (Giugliano and Millward 1987) and one very recently
with a zinc-deficient infant (P.J. Aggett and T. Stack, personal communication)
indicate that a decline in zinc status is accompanied by marked increases in
protein turnover rate. Such effects require confirmation and thus their full
significance is not yet known. However, it is clear that such a metabolic lesion
might well account for the particular rapidity of responses to zinc depletion
seen in young growing subjects (or tissues). It would also limit expression of
growth potential.