SUMMING UP
The present investigation on the stress physiology of skeletal muscle has brought forth some interesting results under conditions of internal irradiation, denervation, work-overload and adenocarcinoma. The growth metabolism of normal muscles in mouse and chick provide reference patterns for the study of alterations induced in various biochemical parameters. Whereas some of the experimental findings embodied in this thesis reaffirm certain aspects of muscle metabolism, other observations open up new avenues for further research on the regulatory mechanisms that are triggered or inhibited during the different stress conditions imposed on the tissue.

Increment in muscle mass results primarily on account of the synthesis and accumulation of structural (acidic) proteins through transcriptional and translational activities of nucleic acids (both DNA and RNA) which are in turn modified or inhibited by basic proteins from time to time during muscle growth. Towards the early stages of postnatal growth when its mechanical activity is negligible, skeletal muscle does well to generate energy for protein synthesis through glycolytic pathway but as the functional demands made on the contractile tissue gradually increase with advancement of growth, oxidative metabolism differentiates rapidly to step up energy generation.
During postembryonic growth, skeletal muscle suffers an overall depression in its glycogenolytic and glycolytic metabolisms owing to decline in the activities of phosphorylases (synthesis and degradation), phospho-
hexose isomerase and aldolase. Growth related increase in succinate dehydrogenase levels indicates an elevated oxidative metabolism for higher energy generation to meet the greater functional demands of muscular tissue towards advanced stages of growth. Transamination products of amino acids contribute to oxidative metabolism at the later stages of muscle growth.

For the last about three decades the absence of the enzyme glucose 6-phosphatase in skeletal muscle has been accepted by the biochemist and as such no work has been attempted on this enzyme in the tissue. The emergence of high levels of glucose 6-phosphatase inhibiting glycogen metabolism in skeletal muscle appears to be a highly significant step in the regulation of carbohydrate derived energy production in the tissue. The role of this enzyme during conditions of stress fortifies the belief and clearly shows that the skeletal muscle has the capability to split up glucose 6-phosphate resulting in the blocking of the later steps in the glycolytic cycle. Also, the
enhanced glucose 6-phosphatase activity resulting in the
depression of glycolytic metabolism in the muscle, coincides
with a corresponding change in the rate of oxidative
metabolism of the tissue. It is an attractive possibility
that glucose 6-phosphatase plays a pivotal role in
controlling the switchover from glycolytic to oxidative
mode of energy production. Need for more systematic study
of this enzyme in skeletal muscle is emphasized through
the present findings.

Skeletal muscle can no longer be considered a radio-
resistant tissue. The muscles studied present a dose-
dependent response to internal irradiation. *M. diaphragm*
is more radio-sensitive than *M. gastroenemius*. Radiation
insult immediately depresses the activities of phospho-
rylases (synthesis and degradation), phosphohexose isomerase
and aldolase and, the conservation of carbohydrates leads
to glycogen accumulation. Significantly elevated glucose
6-phosphatase activity inhibits glucose channelization into
glycolysis and makes available larger bulks of glucose for
the synthesis and accumulation of glycogen. The low
activities of acid and alkaline phosphatases strongly
emphasize that the glucose 6-phosphatase activity studied,
is muscle specific. In the event of carbohydrate
conservation, the utilization of amino acids for energy generation in muscle increases.

The denervated muscle initially attempts to conserve its glycogen through depressed glycogenolysis owing to elevated glucose 6-phosphatase. With the progression of atrophy, glucose 6-phosphatase declines and the elevated phosphohexose isomerase and aldolase levels reveal that denervated muscle ultimately becomes more dependent on the glycolytic mode of energy generation. Oxidative metabolism in denervated muscle remains low and the transamination products are utilized in the glycolytic metabolism rather than the oxidative metabolism towards later stages of investigation.

Work-overload stress results in rapid depletion of muscle glycogen and the activities of phosphorylases (synthesis and degradation), phosphohexose isomerase and aldolase indicate elevated glycolytic metabolism. Later, glycogen metabolism becomes negligible. Relatively low glucose 6-phosphatase activity permits the initially high rate of glycolytic metabolism but later on, the increased enzymic levels depress glycogen utilization. Oxidative metabolism increases continually to support the increased functional
over-load of skeletal muscle. Transamination products of amino acids are thus preferentially used in oxidative metabolism of skeletal muscle under work-overload stress.

The loss of neurotrophic regulation results in the extreme depression of the oxidative capabilities in skeletal muscle and the tissue has to depend upon the glycolytic mode of energy production for its relatively low energy requirements. On the other hand, the muscles under work overload stress resort to greater oxidative effort and the glycolytic mode of energy production is maintained at a significantly low level. In both the stress conditions the channelization of glucose 6-phosphate appears to be blocked because of the elevation depicted in the levels of glucose 6-phosphatase. As such, the bulk of energy in the overworked muscle may be derived from sources other than carbohydrates. Evidently, the oxidative metabolism cannot be stimulated by the denervated muscle in the absence of the neurotrophic factor(s). The elimination experiments can at present provide only the clues to the aberrations induced in the tissue metabolism and any positive knowledge on the neural control of muscle metabolism will be gained only after the neurotrophic factor(s) have been identified.

The present observations on the cancerous state provide irrefutable evidence on the deleterious effects of
tumors on the structure and metabolism of muscle. The
proximity of the tumor site is significant in producing
varying degrees of moderate to severe structural and
metabolic aberrations in muscle. Hypertrophic fibres
identifiable as 'target' and 'targetoid' fibres - a feature
of diseased muscle - are observed under carcinomatous
condition as well. Carcinoma brings about a total loss
of glycogen and, the glycolytic capacity of affected muscle
fibres becomes restricted. At the same time, the alterations
in lipid content and lipase activity reveal a decreased
lipogenesis in muscle on account of the tumor. The
oxidative metabolism of muscle under cachectic condition
is also depressed and the narrow fibres are worst affected
in this regard. The hypertrophied and degenerating fibres
show high acid and alkaline phosphatase activities and
proliferation of connective tissue is indicated in the
muscle as an effect of carcinomatous condition. Whatever
be the fibre-type, it has to suffer degenerative changes
leading to death, sooner or later.