INTRODUCTION
Skeletal muscles exhibit a great deal of biochemical diversity in their metabolism during normal growth and in diseased conditions. The growth of this tissue involves hypertrophy of its constituent fibres as a result of increased rate of protein synthesis. Since the muscle proteins undergo a continual degradation (Millward, 1970 a,b; Gan & Jeffay, 1972) the protein synthetic activity is conceivably maintained at a higher level thereby resulting in a net increment in the growing muscle (Berlin & Schimke, 1965; Goldspink, 1965). As such, the proteins continue to be in a "state of dynamic equilibrium" during the period of active growth as also in steady state (Dreyfus et al., 1960; Winick & Noble, 1965). According to Devi et al. (1963), the rate of protein synthesis is controlled by complementary ratio between DNA and RNA and any change in the nucleic acid content of the tissue reflects upon the rate of protein synthesis and hence the growth rate of the tissue.

Enesco & Puddy (1964) and Moss (1968) have depicted a continual increase in the DNA content concomitant with that in the nuclear population. On the other hand, Malhotra & Katoch (1976b) and Katoch & Malhotra (1978) have demonstrated a discontinuous accretion of nuclear numbers parallel with changes in DNA content of the growing muscle. Any change in DNA levels of the growing tissue reflects upon the transcriptional activity thereby effectuating corresponding alterations in RNA levels (Munro & Gray, 1969; Srivastava & Chaudhary, 1969). The rate of transcription may be further controlled by the inhibitory
mechanisms involving basic proteins, especially histones (Stedman & Stedman, 1950; Bloch & Godman, 1955; Moore, 1963; Spiegel et al., 1970; Weintraub, 1972; Simpson, 1973; Kleinin & Weintraub, 1975). Translational activity for protein synthesis may be controlled by many factors, the most important being the accumulation of structural proteins of the tissue itself (Berlin & Schimke, 1965; Trayer & Perry, 1966).

According to Burleigh (1974), the skeletal muscle during its active growth requires energy for protein synthesis and this energy is derived mainly from carbohydrates stored in the form of glycogen (Munro, 1964; Young, 1970; Griffiths & Rahim, 1978; Newsholme et al., 1978; Newsholme, 1979; Thomson et al., 1979). Thus a continual synthesis and availability of this major energy source becomes fundamental to the growth process. An increased capacity for aerobic metabolism ensures generation of large amounts of energy. Bocek & Beatty (1966), Nystrom (1966) and Asotra & Malhotra (1976) have demonstrated increased rate of oxidative metabolism during muscle growth.

In spite of a large amount of work that has been done to assess the status of glycogen and modes of its synthesis and utilization, very little is known about sequential variations in glycogen metabolizing enzymes during skeletal muscle growth. Most of the literature available on the subject pertains to the study of enzyme systems in the adult tissue (Takeuchi &
Glycogen phosphorylase catalyzes reversible reactions in the directions of glycogen degradation by producing glucose 1-phosphate and in the 'limit dextrin' synthesis by coupling glucose molecule to the glycogen primer, releasing inorganic phosphate. A large number of investigations on normal and diseased muscles have been made to assess the alterations in the phosphorylase activity (Cosmos, 1966, 1970; Cosmos & Butler, 1967; Golisch et al., 1970; Dolken & Pette, 1974; Pette & Dolken, 1975; Pette, 1975; Karpiak et al., 1977; Kitahara et al., 1977; Piehl & Karlsson, 1977), but most of these works pertain to the quantitation of the enzyme for underlining one of its two functions. Also, these investigations have been restricted to a particular stage in the growth of the tissue under normal or diseased conditions. Barring the learned works of Cosmos (1966, 1970) and Cosmos & Butler (1967) on the degradative phosphorylase, any concerted effort to study the dual functioning of phosphorylase during post-embryonic growth and differentiation of skeletal muscle is lacking.
In channelizing the hexose molecule into the glycolytic pathway, glucose 6-phosphate is isomerised into fructose 6-phosphate by the enzyme phosphohexose isomerase. Dreyfus et al. (1968) and Schapira & Dreyfus (1961) related the alterations in the serum levels of this enzyme with the dystrophic condition in skeletal muscle. Study of this enzyme in skeletal muscle has been made by Piehn & Seiler (1976) in adult guinea pig. At present, we are unaware of the sequential changes, if any, taking place in the activity of this enzyme during the skeletal muscle growth under normal and diseased conditions.

Fructose 1,6-diphosphate aldolase is responsible for the formation of triose phosphate molecules leading to the production of pyruvate in the Embden-Meyerhof pathway. Biochemical studies on this enzyme have been made by Prewitt & Salafsky (1967) in cat and by Pette (1975) and Pette & Dolken (1975) in rabbit muscles. Eppelbaum & Kantor (1954) have attempted a study of this enzyme in denervated muscle whereas some investigations on the alterations in the serum aldolase activity in patients with progressive muscular dystrophy have come forth from Sibley & Lehninger (1949); Schapira et al. (1957) and Dreyfus et al. (1958) amongst others. Bergmeyer (1965) has reviewed some of these works.

Glucose 6-phosphate can be converted to free glucose in the presence of the enzyme glucose 6-phosphatase thereby
releasing inorganic phosphate alongwith. Evidently, the enzyme glucose 6-phosphatase does not permit the channelization of glucose 6-phosphate into the glycolytic process and serves as an inhibitor mechanism in energy generation. This enzyme normally present in liver and kidneys is widely reported to be absent in many tissues including skeletal muscle. According to a large number of workers, preparations from tissues other than liver and kidney can catalyze the hydrolysis of glucose 6-phosphate under conditions of glucose 6-phosphatase assay (Swanson, 1950; de Duve, 1953; Harper, 1965). The hydrolase reaction is on account of certain non-specific phosphatases with low substrate specificity. Keeping in view the significance of this reaction in maintaining the glycogen balance (Ryman & Whelan, 1971) an attempt to study the hydrolysis of glucose 6-phosphate in the growing muscle is considered essential.

The significance of acid and alkaline phosphatases in the growth of normal and diseased skeletal muscle has been emphasised by a large number of workers including Beckett & Bourne (1960); Zalkin et al. (1962); Weinstock & Lucas (1965); Pearson & Kar (1971); Kar & Pearson (1972 a,b,c); Gutmann et al. (1976); Katoch et al. (1978) and Malhotra et al. (1978). From the reported literature, it is evident that the acid and alkaline phosphatases are maintained in a balanced state in normally growing muscle and exhibit reciprocal alterations
under conditions of stress (Katoch et al., 1978; Malhotra et al., 1978). The functioning of these phosphatases at pH optima widely different from that of the non-specific phosphatases responsible for the breakdown of glucose 6-phosphate introduces a significant factor necessitating further investigations of these hydrolase systems.

Amino acids undergo transamination to form keto-acids which are channelized into the Kreb's tricarboxylic acid cycle thereby contributing to the energy generation in the muscle. Aspartic acid and alanine constitute the major bulk of protein residues participating in this process. The transamination of these amino acids has been extensively investigated (reviewed by Greenberg, 1969) in the adult skeletal muscle. Studies on the glutamate pyruvate transaminase and glutamate oxaloacetate transaminase in the sera and skeletal muscle of dystrophic patients and animals (Soltan & Blancaer, 1954; Siekert & Fleischer, 1956; Pearson, 1957; Ritter & Seligson, 1957; Murphy & Cherniak, 1958; Dreyfus et al., 1958; Weismann, 1959 a,b; Wentink et al., 1974; Kumar & Rawat, 1976; Matsuda et al., 1978) have contributed to our present day knowledge of the subject pertaining to diseased conditions in skeletal muscle. Since the transamination reactions serve as important indices to the degree of participation of amino acids in energy production, a systematic study of the sequential alterations in the levels
of these enzymes during growth of normal and diseased muscle is considered pertinent.

As already pointed out, the rate of protein increment during muscle growth demonstrates a direct correlation with the oxidative capabilities of the tissue and any study of the enzymic regulation of muscle growth would remain incomplete without determination of the rate of oxidative metabolism. Because of its key position in the Kreb's tricarboxylic acid cycle and its relation with the electron transport system, the enzyme succinate dehydrogenase has been selected for the present investigation.

The response of skeletal muscle to conditions of stress on account of natural disease or experimental induction appears to be all the more complex when studied in light of muscle fibre heterogeneity. In this respect, histochemical approach has an edge over biochemical assays in the sense that the former helps in a qualitative assessment of the response of individual fibre types to the stress factor(s). Numerous investigations have been made in the past to distinguish the muscle fibre types using a large number of morphological and physiological parameters. Beckett & Bourne (1960), George & Berger (1966) and Dubowitz (1974) have reviewed the extensive literature available on the subject.

Metabolic response of the muscle fibre types has been studied histochemically in different myopathies (Cosmos & Butler,
1967; Dubowitz, 1967; Susheela et al., 1969; Dubowitz & Roy, 1970; Douglas & Cosmos, 1974; Jennakens et al., 1974; Tennyson et al., 1975; De Coster et al., 1976; Meijer et al., 1977), in the denervated muscle (Romanul & Hogan, 1965; Drachman & Romanul, 1970; Khan et al., 1973; Shafiq et al., 1974; Sarnat et al., 1977; Dhingra et al., 1978; Katoch et al., 1978; Malhotra et al., 1978) and under work overload conditions (Edgerton et al., 1969; Barnard et al., 1970a,b; Faulkner et al., 1971; Baldwin et al., 1972, 1973, 1975; Romanul et al., 1974; Fette et al., 1975; Tomanek, 1975; Katoch, 1976). Very little, if at all, is known about the metabolic changes in the muscle fibres under carcinomatous conditions (Henson, 1974) although, some work in this direction has come forth in the recent past (Lundholm et al., 1976; Young, 1977; Costa, 1977; Bagwell & Fergusson, 1980). Because of the possible diagnostic significance envisaged, a histochemical investigation on the response of fibre types under cancerous conditions has been included in the present experimentation. The studies have been carried out on three muscles in swiss albino mouse carrying adenocarcinoma tumor.

The present thesis includes studies on the growth metabolism of the swiss albino mouse and chick muscle systems involving six experiments. The experiments, as have been performed, are briefly as follows:
Experiment 1: Studies on the growth of mouse muscle

This includes quantitation of glycogen, proteins (acidic and basic), deoxyribonucleic acid, ribonucleic acid, and succinate dehydrogenase activity in seven muscles at six stages of postnatal growth extending to a maximum age of 15 weeks. The experiment has been performed to obtain a model for the rate of protein increment in relation to the other parameters studied.

Experiment 2: Effect of internal irradiation (Ca$^{45}$) on enzymic levels in mouse muscle

Effect of irradiation on glycogen and glycogen metabolizing enzymes has been studied in diaphragm and gastrocnemius muscles of swiss albino mouse using two different dose rates of radiocalcium (1 uCi and 2 uCi/g body weight). The study has been conducted at six stages up to a maximum post-irradiation period of 28 days. The enzymic parameters investigated include phosphorylase (degradation), phosphorylase (synthesis), phosphohexose isomerase, non-specific phosphatase hydrolysing glucose 6-phosphate under conditions of glucose 6-phosphatase assay, acid phosphatase, alkaline phosphatase, glutamate pyruvate transaminase and glutamate oxaloacetate transaminase. Normal controls have been studied alongwith.
Experiment 3: Studies on the glycogen metabolism in chick skeletal muscle

This experiment includes biochemical studies on the alterations in the glycogen content of the chick gastrocnemii muscles (pars externus, medius and internus) at nine stages of post-embryonic growth extending to a maximum period of 9 weeks posthatching. Corresponding changes in the activities of the enzymes phosphorylase (degradation), phosphorylase (synthesis), fructose 1,6-diphosphate aldolase; phosphohexose isomerase, non-specific glucose 6-phosphatase, glutamate pyruvate transaminase, glutamate oxaloacetate transaminase and succinate dehydrogenase were recorded at these stages in the normally growing muscles under investigation.

Experiment 4: Studies on the glycogen metabolism of denervated chick skeletal muscle

Unilaterally sciatic-tomized chick gastrocnemii were studied for the alterations induced in the glycogen levels at weekly intervals for a maximum period of 9 weeks post-denervation. Studies on the changes in the levels of various enzymes mentioned in Experiment 3 were made at corresponding stages.

Experiment 5: Studies on the effects of work-overload on the glycogen metabolism of chick skeletal muscle

This experiment involves biochemical assays of glycogen and the related enzymes in the gastrocnemii muscles of the
contralateral limb in the animals subjected to denervation procedure under Experiment 4. The study has been conducted to assess the alterations in the glycogenolytic system under work-overload stress.

Experiment 6: Effect of adenocarcinomatous growth on the histochemical profiles of the skeletal muscle

The experiment involves induction of adenocarcinoma by transplanting tumor tissue from naturally tumor-bearing mice. The effect of cancerous condition on the metabolism of red and white types of muscle fibres was studied with respect to the histochemical localization of glycogen, lipids, phosphorylase, aldolase, lipase, succinate dehydrogenase, cytochrome oxidase and acid and alkaline phosphatases. The muscles selected for the investigation include *M. triceps*, *M. pectoralis* and *M. gastrocnemius*.

Chapter 1 of this thesis incorporates the results and discussion pertaining to Experiment 1 whereas Chapter 2 includes the studies on the irradiated skeletal muscle as already mentioned. Chapter 3 incorporates three experiments involving studies on the normal, denervated and over worked chick *gastrocnemii*. Chapter 4 pertains to the histochemical studies on the carcinomatous skeletal muscles in swiss albino mouse.