CHAPTER 1
Diabetes and obesity are well known problems associated with dysfunction of neural and hormonal system, that oversee the energy balance. The control of autonomic nervous system and adrenal on body weight and body composition has been illustrated in this chapter. Rats were subjected to vagotomy (VGX), adrenalectomy (ADX) and vagotomy and adrenalectomy together (VGX + ADX). Vagotomy resulted in slight but not significant increase in body weight. Liver water content decreased in these rats which could be the reason for the decrease in liver weight. But, adrenal glands showed hypertrophy favoured by enhanced ACTH activity. Bilateral adrenalectomy decreased the body weight whereas the weight and percentage water content of the liver increased in response to deprived cortical and medullary hormones. Increased liver weight could be due to increased glycogen and lipid depots in the liver. Total adrenalectomy cannot withstand stress condition and leads to death over a long period. Within the experimental period in the rats subjected to VGX + ADX simultaneously, body weight, liver weight and percentage water content decreased noticeably.

Guanethidine induced chemical sympathectomy (CSX) decreased body weight along with increase in liver weight and water content of the liver. Similar results were noticed in rats treated for sympathectomy and vagotomy together (CSX + VGX). Compared to liver, the reverse were the alterations in the adrenals. Adrenal glands decreased in size and weight in both CSX and CSX + VGX rats compared to their respective controls. In the animals treated for chemical sympathectomy and adrenalectomy together (CSX + ADX) body weight
increased slightly, as a result of persisting parasympathetic tone. But liver weight and water content of the liver decreased compared to that of the controls. These rats became very weak and lethargic and invariably leads to death if kept for longer period. Thus, it can be concluded that neural and hormonal system interact amiably to maintain energy balance.

CHAPTER 2
Glucose is the predominant metabolic fuel of the central nervous system. The glucose homeostasis is maintained in the normal range by the neural and hormonal system of the body. The control of glycaemia by parasympathetic component of autonomic nervous system and endocrine glands (adrenal) was investigated and the result is discussed in this chapter. Vagal dysfunction or vagal ablation resulted in profound hyperglycaemia with a concomitant decrease in glycogen stores and glycogen synthase activity in the liver. Activities of enzymes involved in glycogenolytic pathway [viz., glycogen phosphorylase and glucose-6-phosphatase (G-6-Pase). Succinate dehydrogenase (SDH) activity was enhanced thereby rendering hyperglycaemic condition. Lactate dehydrogenase (LDH) activity also showed an increase denoting increased glucose utilization. Vagal sectioning declined the activity of AchE, which is the enzyme that removes the parasympathetic neurotransmitter.

Bilateral adrenalectomy caused a low blood sugar level after 48 hrs. Tissue glycogen content increased in these animals with a simultaneous increase in glycogen synthase activity. On the otherhand, Glycogen phosphorylase and glucose-6-phosphatase activities decreased noticeably, which could be the reason for the observed hypoglycaemia. AchE activity increased compared to that of sham operated animals.

Rats operated for vagotomy and adrenalectomy together, showed only a marginal hyperglycaemia. In these rats tissue glycogen content decreased but glycogen phosphorylase and synthase activities increased parallely. Glucose-6-phosphatase activity increased slightly compared to the rats of sham operated group. LDH and SDH activities decreased noticeably in VGX + ADX rats.

Parasympathetic system, thus is seen influencing glucose uptake by liver cells while adrenal hormones are involved increasing glycaemic level. Adrenalectomy was partially successful in counteracting the effects of vagotomy.
CHAPTER 3

The role of parasympatho-adrenal axis on the regulation of metabolic activities of rat liver has been highlighted in this chapter. Rats were subjected to surgical operations for vagotomy (VGX), adrenalectomy (ADX) and vagotomy+adrenalectomy (VGX + ADX). After 48hrs, various biochemical parameters were estimated in the liver of overnight fasted animals. Vagotomy resulted in enhanced proteolysis and lipolysis, thereby favouring the hyperglycaemic state. Activities of various phosphatases (acid, alkaline and Na⁺-K⁺ ATPase) declined compared to that of sham operated animals. Activities of both (ALT & AST) increased which could provide substrates for gluconeogenic activities.

Removal of both the adrenals which diminished the cortical and medullary hormones, led to varied metabolic disturbances. Tissue protein content increased slightly with a significant increase in acid phosphatase activity. Lipid depots decreased scarcely compared to sham operated animals. Whereas, membrane bound enzyme activities decreased in the liver of adrenalectomized rats compared to that of sham operated rats. This could mean that the transport of metabolites across the membrane is decreased.

Rats operated for vagotomy and adrenalectomy together does not show much alterations in the protein and lipid contents of the liver. Alkaline phosphatase, Na⁺-K⁺ ATPase and aspartate transaminase activities declined markedly compared to that of the rats of sham operated group. However, alanine transaminase and acid phosphatase activities increased slightly but increase is nonsignificant compared to that of sham operated animals.

Vagotomy, thus reduced glucose uptake across liver cell membrane, storage of metabolites and reduction in glycolysis. Adrenalectomy produced opposite effect. When vagotomy combined with Adrenalectomy the metabolic reactions did not alter much. In other words vagotomy effect was to some extend counteracted by adrenalectomy.

CHAPTER 4

Liver is the central organ of metabolic homeostasis regulating carbohydrate metabolism. Metabolic reactions in the liver are governed by an interplay of sympathetic and parasympathetic nervous system and endocrine glands. Manipulation of sympathetic system is rendered by Guanethidine sulphate, a antisympathetic drug. Chemically sympathectomized
rats (CSX) showed hypoglycaemic state with a parallel increase in glycogen stores in the liver. Glycogen phosphorylase, G-6-Pase, LDH and SDH activities decreased compared to those of rats of the control group. Under the influence of activated parasympathetic tone (CSX rats) glycogen synthase, and AchE activities increased in the liver.

The hypoglycaemic state of sympathectomized rats got more pronounced when adrenalectomy was also performed simultaneously in them (CSX + ADX). The various metabolic parameters showed similar trend as was seen in only sympathectomized rats (CSX).

However, when chemical sympathectomy and vagotomy were executed together (CSX + VGX) only a marginal hyperglycaemia was observed. Tissue glycogen content, glycogen synthase and glycogen phosphorylase activities declined. However, G-6-Pase and LDH activities showed slight increase. AchE activity declined in these rats suggesting a suppressed parasympathetic tone. The results show that the hyperglycaemic condition produced by vagotomy can be nullified to some extent by chemical sympathectomy.

CHAPTER 5
Flux rates through metabolic pathways, may be governed by regulatable enzymes on the pathway and by metabolic channelling of substrates leading to metabolism by one pathway in preference to another. The activities of some of these enzymes is also under the control of autonomic nervous system. Chemically sympathectomized rats showed high protein and lipid stores of the liver which is followed by enhanced acid phosphatase activity. Whereas, alkaline phosphatase, Na+K+ ATPase and transaminases (AST and ALT) activities decreased in these rats. Moreover, identical results were noticed in rats subjected to chemical sympathectomy and adrenalectomy in combination (CSX + ADX). The expression of enzymes was more pronounced in these rats. Even total lipid stores increased prominently. While total protein content showed the reverse result.

Rats subjected to chemical sympathectomy and vagotomy together (CSX + VGX) showed varied results. Total protein and lipid content declined compared to the control group rats The activities of the phosphatases also declined in these rats suggesting a reduced transfer of the metabolites across the membrane. Alanine transaminase decreased favouring a reduced gluconeogenesis and which in turn might have caused the hypoglycaemic condition.
Thus, the influence of sympathetic and parasympathetic systems on the regulation of various metabolic pathways is of prime importance to attain metabolic homeostasis. The effect of parasympathetic nerves on the metabolic reactions is more pronounced than that of the sympathetic system.

CHAPTER 6
Mammalian glucose homeostasis is partially controlled by glucose sensor mechanisms in the endocrine pancreas and partially through autonomic nerves. The influence of the autonomic nervous system on pancreatic insulin secretion has been studied in the present study. Vagal sectioning decreased serum insulin significantly compared to that of the sham operated rats which could be the reason for the resulting hyperglycaemic condition prevailed in these rats. Bilateral adrenalectomy and chemical sympathectomy singly (ADX & CSX, respectively) increased insulin level to the same extent. Even, when vagotomy was performed together with adrenalectomy (VGX + ADX), insulin level declined but this decrease is not as significant as in only vagotomized rats. Similar result was obtained with rat treated for chemical sympathectomy and vagotomy together (CSX + VGX). This slight decrease could favour marginal hyperglycaemia.

On the contrary, serum insulin level increased severely in rats treated for chemical sympathectomy and adrenalectomy simultaneously, a reason that could be ascribed for severe hypoglycaemia present in these rats. These results indicate the importance of sympathetic and parasympathetic nerves in the secretory activity of endocrine pancreas. Parasympathetic fibers induces insulin secretion and removal of adrenergic influences (CSX + ADX) decreases the release of insulin.

CHAPTER 7
The autonomic nervous system is known to influence the status of thyroid hormone through complex ways. Thyroid hormones in its influence a variety of metabolic parameters in many tissues. In vagotomized rats (VGX) hormones were found to increase. Serum T₃ level increased markedly with a concomitant decrease in T₄ and TSH level compared to sham operated rat. This increase in T₃ level could be due to triggered deiodination of T₄ to T₃. Following adrenalectomy (ADX) thyroid status was similar as obtained in vagotomized rats but the changes were not as significant as in vagotomized rats. But in VGX + ADX rats
serum $T_3$ and $T_4$ level increased parallely and TSH level declined when compared to that of the sham operated rats.

Guanethidine induced chemical sympathectomy (CSX) declined thyroid status. Serum $T_3$ and $T_4$ level decreased while TSH level increased in these rats compared to the rats of control group. These alterations in thyroid hormones and TSH level was more pronounced when adrenalectomy was also performed along with chemical sympathectomy (CSX + ADX). Such a condition favoured a reduced transport of glucose resulting in severe hypoglycaemic condition. However, in CSX + VGX rats, serum $T_3$ and TSH level declined significantly along with nonsignificant increase in $T_4$ level. Overall thyroid status declined in these rats. Thus, it can be concluded that neural and hormonal system together regulate thyroid status in a dramatic way. Also, the hypo- and hyper-thyroidic conditions has disparate effect on liver metabolism and in turn on glucose homeostasis. The effect of autonomic nervous system and adrenal hormones on glycaemic conditions manifest partially through their secondary influence on thyroid hormone release from thyroid gland.

CHAPTER 8

A multitude of intrinsic physiological relationships carefully regulate and fine tune the homeostasis, of which insulin has a vital role and is controlled by three major factors: the nervous system, hormones and metabolites. In vagotomized rats the significant hyperglycaemia was observed at 0 min. which reached the zenith within 15 min. after the glucose load. Even upto 150 min. baseline glucose level was not attained. This was mainly due to decreased serum insulin level compared to sham operated rats. Similar, Glucose tolerance curve and pattern of insulin response to glucose load was observed in VGX + ADX rats. However, in adrenalectomized rats persisting parasympathetic tone manifest its glucoregulatory influence after glucose level peak was attained. This is supported by a simultaneous increase in insulin level as in sham operated rats after glucose injection. Thereafter, glucose level reached the baseline level by 150 min. Even, serum insulin level declined to the one at 0 min. in both sham and experimental group. A similar pattern of glucose and insulin curve was observed in rats subjected to chemical sympathectomy singly (CSX) and in combination with adrenalectomy (CSX + ADX). In both the cases vagal control is highlighted. Thus, serum glucose level after attaining the peak at 30 min. declined gradually to baseline. On the contrary, in CSX + VGX rats glucose level continued to remain high till
150 min. compared to sham operated in which it reached the baseline. Serum insulin level remained low throughout, but control group rats showed the peak at 30 min., and a nadir at 150 min. Thus, parasympathetic action is very much required for proper response to hyperglycaemia. The cholinergic activation in diabetic condition along with suppression of adrenergic system could bring the normal pattern of glucose tolerance.