The exoWAT, endoWAT and ectoWAT Dictate Dysmetabolism, Dyslipidemia & Diabetes

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BACKGROUND
Standard 75-gram, two-hour OGTT along with insulin levels was used in over 2000 individuals and the data was analysed in the exoWAT, endoWAT and ectoWAT. The beta cell and the proposed 'Delta-Gamma system' physiology of pancreatic islet, hypothalamus, gut and peripheral tissues regulating the carbohydrate, fat, protein and energy metabolism. (Fig.1)

MIDDLE TIER
The beta cells regulate anabolism mainly by secreting insulin, glucagon and amylin. Uncontrolled gut-brain axis to secrete somatostatin (SST) and amylin stimulates gamma cells to secrete pancreatic polypeptide (PPY), SST inhibits glucagon which controls glucose and protein catabolism. PPY inhibits glucagon which controls lipid catabolism. Glucagon and glucocorticoids inhibit beta cells. Thus the 'Delta-Gamma system' controls catabolism very much like an 'electronic' 'brake-fuel' system. (Fig.2)

ENERGY ACQUISITION:
• Gluconeogenesis
• Fat → Cholesterol → GIP
• Carbohydrates → GIP

ENERGY STORAGE:
• Glucose → Glycogen
• Fat (DNL) → endoWAT
• Protein → amino acids & proteinase

ENERGY EXPENDITURE:
• Cellular respiration – muscles, heart
• BAT thermogenesis
• Insulin → WAT & liver

HUMAN BIO-ENERGETICS
It deals with acquiring and storing energy as well as utilizing it for the processes. (Fig.3)

ENERGY STORAGE
ROLE OF INSLIN & LEPTIN
WAT generates adiponectin and leptin. Adiponectin has critical role in FFA to non-muscle and liver. Leptin has 4 actions:
• Stimulates insulin secretion by beta cells
• Inhibits growth hormone and causes satiety by hypothalamic secretion
• Modifies gut incretin secretion.
• Stimulates mitochondrial triglyceride transfer protein (MITTP) in hepatocytes. (Fig.3)

ENERGY EXPENDITURE
Normal metabolism
• Lipolytic stage
• Normal metabolism
• Peripheral ectoWAT

GENETIC IR
Genetic IR predisposes to diabetics. Genetic hyperIR presents with fasting hyperglycemia & HbA1c. Genetic IR presents with PP hyperglycemia & IR → T2D. Genetic IR being obesity-resistant presents as the hyperglycemia phenotype of T2D. This analysis helps to make a rational choice of anti-diabetic therapy.

FIG. 4

OGTT & INSULIN RESISTANCE
The hyperinsulinemia observed during euglycemic hyperinsulinaemia is a physiological phenomenon and is an adaptive response to increasing amounts of DNL. Increased endoWAT and does not qualify the use of term, 'insulin resistance'. However, the euglycemic accumulation in liver and peripheral tissues does constitute the actual insulin resistance. The endoWAT drives dysmetabolism and endoWAT-like phenotype by the ectoWAT drives dysglycemia. During and after lipolytic stage, continued calorie surplus causes 'organ IR' which does not fall till the end of the euglycemic accumulation continues to perpetuate T2D. However, cancer restriction and barriers surgery maybe effective over a period of weeks but requires at least a year to deplete peripheral ectoWAT.

FIG. 5b

CONCLUSIONS
• OGTT with insulin levels is a very useful tool to study the kinetics of glucose and insulin and risk stratify the stage of dysmetabolism.
• The three tier model proposes to explain the physiology of normal metabolism, the Delta-Gamma system, the Delta-Gamma system to control the basal metabolism in a flip-flop manner. Insulin controls the MITTP metabolism.
• Leptin & growth hormone stimulate and lipolysis and leptin controls the hepatic excess leads to DNL, generating endoWAT which is the cost of dysmetabolism, dyslipidemia and dysglycemia.
• Ectopic WAT causes 'organ insulin resistance' and leads to dysmetabolism.
• Dysmetabolism timeline is proposed which will help to stratify and help the medical patient. It will help in the clinical management of T2D, prediabetes, metabolic syndrome, MAFLD, cancer fatality and diabetes. Will be helpful in the clinical diagnosis of metabolic syndrome.
• Serial assessment will be useful in monitoring intervention and several measures.

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FIG. 6

Please visit our OGTT-PLUS calculator @ www.ogtt.in

Fig. 3

Fig. 4

Fig. 5b

Fig. 6

Fig. 5a

Fig. 7