

SECOND ADVANCED COURSE IN DIABETES MELLITUS

November 2 to 7, 1985

All India Institute of Medical Sciences, New Delhi

This 40 hour course comprised of didactic lectures, clinical conferences and case demonstrations. An attempt was made to cover recent advances in basic sciences, new information in the field of diabetes in allied sciences and the rationale for use of new innovations in therapeutic measures as applicable to our country. A Faculty of 20 specialists was inducted to conduct this course.

A resume of the topics covered is presented under the following headings :

- * Basic Sciences.
- * Clinical aspects.
- * Specialities and Diabetes (obstetrics, paediatrics, psychiatry, surgery).
- * Clinical conferences (clinicopathological conference, therapeutic conference, radio-logical conference).
- * Case demonstrations (patient management problems; nutritional planning).

Following are the extracts of new information from each presentation.

BASIC SCIENCES

Insulin and its secretion : (R.L. Bijlani, R.J. Dash)

The synthesis of insulin was sequenced, from the level of mRNA until emicytosis. Calcium is required for microtubular contractile function, which facilitates movement of granules from the interior to the surface of the cell.

Insulin secretion depends both upon the presence of substrates (glucose, aminoacids, fatty acids, gut hormones) and neural influences (sympathetic and parasympathetic).

Insulin release occurs in two phases : the first, which is not related to prestimulation glucose level and the second; which is threshold related.

The two chains of the insulin molecule are connected by a 31 aminoacid link, the C-peptide (mol. wt. 3021). C-peptide occurs in equimolar concentration to insulin. During intraportal passage of C-peptide there is negligible extraction by the liver. Only 1-4% of the total C-peptide is excreted in the urine.

Intravenous administration of glucagon can be used to determine, the- C-peptide reserve. We concentration of C-peptide in insulin dependent diabetes mellitus (IDDM)

is about 1.9 ng/ml, while in non-insulin dependent diabetes mellitus (NIDDM) it is usually more than 20 ng/ml. Sufficient C-peptide reserve indicates that the patient can be managed by diet or oral hypoglycaemic drugs.

The weight of the pancreas and total mass of endocrine tissue in the two types of diabetes is as follows :

	Wt. of pancreas gm.	Total mass (endocrine tissue) mg.	Lobe rich in PP cells
Control	82	1395	11.1
Type I (IDDM)	39.75	433	20.6
Type II (NIDDM)	73.25	1449	13.5

After the sixth decade, the immunoreactive insulin (IRI) levels begin to decrease.

Proinsulin normally constitutes less than five percent of the total circulating insulin. The proportion further diminishes after glucose load. Elevated levels of proinsulin (> 10%) are more suggestive for insulinoma. This is irrespective of the extent of low blood glucose value recorded during hypoglycaemia.

Etiopathogenesis of complications (G.P. Sharma, N.P.S. Verma)

Pathogenetic mechanisms for atherosclerosis and microangiopathy leading to vascular complications were reviewed. The initiating event in atherosclerosis is endothelial injury, which is followed by platelet adhesion, aggregation and high levels of beta thromboglobulin. Arterial smooth muscle proliferation and lipid accumulation (receptor pathway) add further to increase the resistance of vessel wall and its susceptibility to the thrombogenesis.

Microvascular involvement is associated with glycosylation of proteins, cross linking with immunoglobulins (glomerular deposits) accumulation of sorbitol (through aldose reductase enzyme pathway), loss of pericytes, causing leakage, transduction from capillaries and development of microaneurysms (retina).

Mortality data of diabetes from the Irwin Hospital, 1983-84 New Delhi, was presented to illustrate the natural history of the disease in our country.

Cardiovascular deaths	--	21.2 %
Cerebrovascular deaths	--	12.6 %
Renal failure	--	22.5 %
Diabetic coma	--	21.2 %
Hypoglycaemia	--	4.0 %
Infections	--	5.4 %

In the field, causes of death were myocardial infarction 3.57 %, chronic renal failure 20.43%, cerebrovascular accidents 17.8%, tuberculosis 7.14%, other infections 3.9% and coma 3.6 %. The mean duration of diabetes was 13 yrs, and the mean age at death 63 yrs.

Platelet function in Diabetes (A. Dindi)

Platelets contain alpha granules, dense granules and lysosomes. Alpha granules comprise of fibrinogen, factor V, PF4-heparin, beta thromboglobulin and prostaglandin F; dense granules contain ATP, ADP, pyrophosphates, serotonin and calcium while lysosomes contain acid hydrolysases.

Platelet abnormalities in vasculopathies include (a) increased activity of the enzymes endoperoxidase, prostaglandin synthetase, (b) increased arachidonic acid content of platelet phospholipid and (c) increased platelet turnover.

The sequence of platelet receptor changes, and thrombi formation leading to endothelial injury was illustrated. In vitro and in vivo tests for evaluating platelet function were described.

Lipid metabolism (D. R. Siddharth)

The metabolism of various lipid constituents were discussed (cholesterol, phospholipids, triglycerides, free fatty acids). The interrelation of lipoproteins and apoproteins is as given below.

<i>Lipid fraction</i>	<i>Apoprotein</i>
Chylomicrons	B.C.E.
HDL (alpha)	A ₁
LDL (Beta)	B
VLDL (pre-beta)	C.E.

Type IV hyperlipoproteinaemia (VLDL) was present most often in Indian diabetics, followed next in frequency by Type Iib (LDL and VLDL).

The lipid abnormalities in IDDM and NIDDM were distinctive. Low HDLc was not an important risk factor for coronary artery disease in Indian diabetics, while VLDL appeared to be significant here as a risk factor for vascular disease.

Autoimmunity in Diabetes (A.N. Malaviya)

The autoimmunity was referred to as immunoinflammation, which is consonant with persistent inflammation and tissue damage. Antigen reacts with the genetically recognised receptor, involving interleukin I, helper T cells, and interleukin II. This

results in excitation of cytotoxic T cells, and further involvement of plasma cells giving rise to antibodies and antibody dependent cytotoxicity. In the early phase of IDDM, islet cell antibodies are present in 70 to 80% of patients but after 5 years the positivity decreases to 15-20%.

The IgG which is initially non-complement fixing becomes complement fixing, thus leading to activation of complement cascade and tissue damage (vasculitis, neuropathy, nephropathy).

Genetics of Diabetes (N.K. Mehra)

Human leukocyte antigens on the short arm of chromosome six--class I. A,B,C loci (present in all nucleated cells) class II. DR (found in lymphocytes and macrophages, Irg) and class III Bf, C₂C₁, were described. The association of diseases, especially endocrine with HLA (B8, B15, BW49, DR3, DR4) was delineated. In North India the relative risk (RR) for DR3 was higher in IDDM (RR 10.52-78.4% in patients, 25.7% in control).

DR3, B8 had lower IBC, persistent ICA and ICF, in contrast to DR4 B15 with increased IBC and transitory ICA and ICF.

Among North Indian multiplex families of diabetes, HLA was identical in 72.5% and haplotype was identical in 27.5%. DR2 B7 A3 was protective against diabetes in the population as elsewhere. In the diabetic group, a PH 18 kilobase DNA restrictive fragment was seen associated with DR3/DR4, while in the controls (non-diabetics) it was Ben 3.7 kilobase fragment.

CLINICAL ASPECTS

Epidemiological studies (K. Ramachandran)

Epidemiology is defined as the study of distribution and determinants of disease. The predictive value of screening was described as related to sensitivity, specificity and accuracy. Epidemiological studies are sequentially formulated as follows.

- I. Identification of the problem. Identification Of potential role of risk factors (descriptive studies).
- II. Test of hypothesis, role of risk factors (analytic studies).
- III. Ancillary evidence to strengthen confidence in observations and association (consistency, biological plausibility).
- IV. To perform experimental studies if feasible or ethical (experimental observations).
- V. Design and test practical (controlled trial).

Cardiovascular disease (H.S. Wasir)

Even in the absence of cardiovascular involvement, Vo₂, max. in the diabetics is not in the normal range.

Impaired glucose tolerance test (IGT) was qualified partly as false negative diagnosis of diabetes, or IGT in transition to diabetes. It is well recognized that even in IGT stage vascular disease occurs. The vascular involvement in diabetics is premature and in severity more extensive. Hypertension, usually of the low-renin type occurs in 40-80%, of diabetics. Some of the drugs used in cardiovascular disorders must be used with caution in diabetics, e.g. due to the presence of autonomic neuropathy in diabetics, nitrates would cause a further fall of cardiac output, and postural hypotension;

-beta blockers can produce cold extremities, while thiazides can worsen further the glycemic state.

Peripheral vascular disease (M. Sheik)

In peripheral vascular disease findings observed by Doppler sonography were substantiated by angiography in 80-90%. The clinical symptomatology is, however, misleading (clinical suspicion collaborated with Doppler findings only in 30%).

In diabetes, on angiography there was multiple segmental, diffuse involvement often below the knee. In contrast peripheral vessel involvement among non-diabetes was often unilateral and monosegmental. Involvement of aorta, iliac and femoral vessels was frequent while the leg vessels were usually spared.

Renal disease (B.R. Sengupta)

Severity of clinical profile has no consistent relationship to histopathological findings. Overt clinical features may not develop even with fairly advanced histological changes.

Clinical staging is suggested as follows :

- * Reversible elevation of "GFR.
- * Intermittent proteinuria (> 20 mg/dl).
- * Persistent proteinuria (selective) > 1.g/24 hours.
- * Renal failure-end-stage renal disease.

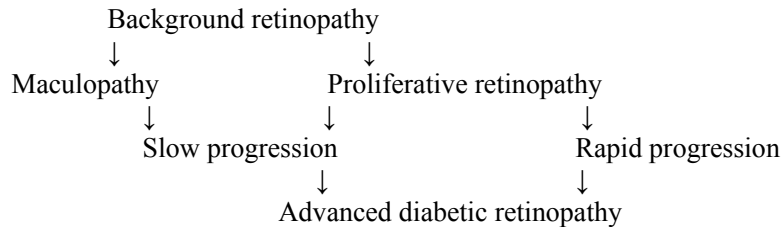
It was contended that proteinuria in diabetics does not always progress to renal failure.

The association of hypertension (hyporenin hypoaldosteronism), glycaemia (increased insulin sensitivity), renal retinal syndrome (K.W. syndrome with retinal involvement), anaemia (erythropoietin depression) and clotting defects (Guanine prostacycline excess, thromboxane deficiency) was discussed. Again, impaired defense mechanisms, autonomic neuropathy and microvascular disease increase its susceptibility to urinary tract infections. Acute pyelonephritis was three times as common, and asymptomatic bacteruria four times in diabetics compared to non-diabetics.

The incidence of diabetic nephropathy appears to increase after a mean duration of ten years. Males are more often affected than females.

Ophthalmic Changes (P.K. Khosla)

The natural history of retinopathy is depicted as follows :



The advantages of fluorescein angiography in diabetes are (1) objective assessment of retinal status, (2) detection of vessel involvement even when routine fundoscopic appearance is normal (3) in maculopathy exact location can be determined (4) progression of background retinopathy to the proliferative variety can be evaluated (5) proliferative and feeder vessels can be precisely located (6) adequacy of treatment can be objectively judged.

Photocoagulation which may have to be repeated, delays the progress of the disease. It does not generally improve vision, except in maculopathy. The overall five year prognosis for blindness does not appear to be benefited with photo coagulation.

Autonomic Nervous System (Dr. (Mrs.) S.G. Bhatia)

In diabetes, autonomic dysfunction can involve all systems of the body, which can be detected by a variety of diagnostic tests. Subtle clinical features and a number of investigative procedures were subjected to multivariate discriminant analysis, which showed that symptoms such as sweating disturbances, postural hypotension and bladder dysfunction were predominant. In cardiovascular reflexes, absence of sinus tachycardia, 30/15 ratio (< 1.03) valsalva manoeuvre (< 1.21) and absence of response to atropine injections were rated high statistically for diabetics with autonomic dysfunction.

Infection and Diabetes (A. Das Gupta)

This subject was covered under the following headings :

1. Acute infection that can trigger diabetes :

- a) directly by diabetogenic virus, IDDM by destruction of insulin producing Beta cells.

NIDDM-by persistent infection without causing any destruction of insulin producing Beta cells.

- b) indirectly by excessive release of hormones, e.g. growth hormone, glucagon and cortisol.
 - c) E. coli septicaemia leading to hypoinsulinaemia.
2. Diabetes mellitus makes the host susceptible to infection by
 - a) alteration in endocrinologic and metabolic state and by
 - b) Impairment in the defense mechanisms of the host.
 3. Factors that predispose to infection or contribute to susceptibility to infection, common sites predisposed to infection, eg. urinary tract and the respiratory tract.
 4. Common organisms involved in diabetes include indolant type of organisms, leading to chronic infection, eg. tuberculosis, or fungal infections.

The defense mechnisms in diabetics are affected by different factors : a)

- a) Presence of complement, malnutrition.
- b) Leucocyte functions alteration low opsonic activity.
- c) Lymphocyte function
 - Humoral-antibody production,
 - Cellular-Lymphoproliferation response in vitro-K and NK cell cytotoxicity, lymphocyte subpopulation using monoclonal antibodies.

TREATMENT MODALITIES

These were discussed under the following headings :

(H.B. Chandalia S.S. Rastogi, M.C. Srivastava, M.M.S. Ahuja; M.G. Karmarkar)

- I. New insulin and insulin delivery systems.
- II. Pharmacological aspects of oral hypoglycemic agents (OHA), indications for the use of OHA.
- III. New aspects in monitoring, compliance to therapy, transplantation of pancreas.
- IV. Problems during management-Somogyi effect, Dawn phenomenon, insulin resistance.
- V. Management of diabetic metabolic emergencies.

Profile of insulin absorption depends on the type of insulin, and *viz-viz*, insulin concentration in the circulation. 30-40% of injected insulin is in destroyed the

subcutaneous tissue (rarely 90%). Continuous infusion of insulin is recommended for special situations such as pregnancy, maculopathy and diabetic ketoacidosis. The advances in pump therapy and implantable devices were outlined.

Among the newer insulins, biosynthetic and synthetic human insulins provide the advantages of lower immunogenicity, species specificity and greater patient acceptance; PIF pre-proinsulin, which is pure pork insulin with proinsulin <1 ppm, glucagon <0.1, and pancreatic polypeptide <0.01 is to be available in India shortly.

Mechanism of action of oral hypoglycaemic agents, especially new information on extrapancreatic sites of action were described. The choice of a sulphonylurea agent depends on nutritional state, dietetic pattern, presence of concomitant cardiac, renal disease, and drug therapy for other associated disease. Primary and secondary failure were defined and ground for combined therapy indicated.

Regular monitoring of glucose, especially in unstable diabetes, childhood diabetes and diabetes in pregnancy were recommended. Hb A₁ C provides a better index of glycaemic status. Good motivation, provision of facilities for treatment review and subsidized costs of therapy were emphasized for improved compliance.

The present status of pancreatic transplantation, improvement in technique by using a segmental graft and immunosuppression with cyclosporine, and use of appropriate selection criteria were discussed.

Somogyi effect depends on hypoglycaemia: hyperglycaemic response. This is often iatrogenic and could be due to counter-regulatory hormones.

Dawn phenomenon refers to early morning hyperglycaemia. There was evidence that it is related to increased clearance of insulin in early morning, a phenomenon which is seen also in patients on biostator or in IDDM patients on insulin pump therapy.

Insulin resistance was defined more in the context of a state where the biological effectiveness of insulin is reduced. This action is to be interpreted at the cellular level (receptor) and includes all biological effects of insulin (antilipolytic, aminoacid uptake, growth stimulation). Insulin action is quantitated by (a) dose response curve, (b) hormone sensitivity (1/2 max. biological activity), (c) hormone response test (maximum). The causes of resistance were outlined as follows :

State	Binding effect	Receptor conc.	Affinity
Obese diabetes	↓	↓	N
Lean diabetes	↓	↓	N
Insulinoma	Variable	↓	Variable
Acanthosis Nigricans type A	↓ ↓	↓ ↓	Normal
B	↓ ↓	Normal	AB +
C	Normal	Normal	N Post-receptor defect
Acromegaly	N ↑	↓	↑

Specialities and Diabetes

Pregnancy in Diabetes (Kamal Buckshee, V. Seshiah)

Pregnancy in diabetes is associated with an increase of complications, e.g. toxemia, hydramnios, stillbirth, congenital malformation. Neonatal complications are also increased, e.g. macrosomias, congenital malformation, respiratory distress syndrome and unexplained uterine death. The metabolic alterations are directed to increasing anabolism. The single spot blood glucose F > 85 mg, PG > 105 mg% is considered to be a good screening test. Otherwise O' Sullivans criteria are applicable to gestational diabetes (fasting 90 mg%, 1 hour 165 mg%, 2 hour 145 mg%, 3 hour 125 mg%, venous whole blood). In drug management, increase of body weight by 502 g/week (24.25 lbs during pregnancy) and a blood glucose value <105 mg% is considered ideal.

Diabetic women must be properly informed on the use of contraceptives since pregnancy must be planned with implications of various complication that can accompany gestation.

Since intrauterine contraceptive devices have a higher failure rate in diabetics, hormonal contraceptives are preferable. These include combined oral pills, low dose progestogen pill, biphasic and triphasic pills, and injectable hormonal implants. Newer phasic formulations of combined pills are considered better as they are more efficient and the total hormone used per cycle is regulated according to the cycle, which requires a lesser dose than conventional pills.

Childhood diabetes (A. Amini)

Childhood diabetes presents enormous problems in management; e.g. at times it is not detected early because it is so uncommon in the paediatric age group: In therapy, diet is invariably inconsistent, small doses of insulin adjustments seem cumbersome, and hypoglycaemic episodes are very frequent. There is the risk of neuropsychological sequelae due to repeated hypoglycaemia. Children comprise 0.7-2.3 percent of all diabetics attending speciality clinics in our country. Genetic, racial and hereditary factors determine variations in prevalence from country to country. The onset is usually rapid 20% presenting initially with diabetic ketoacidosis. Enuresis, anorexia, abdominal pain, lassitude, fulminant infections that are non-responsive to the usual therapeutic measures are other modes of presentation.

Regarding therapy, insulin requirements tend to increase with time. Often there is poor control due to adverse family background or poor socioeconomic status. If therapy is irregular, growth potential is reduced to <25% percentile.

Psychiatric aspects of Diabetes (Dr. (Mrs.) P. Chawla)

Psychiatric aspects were categorised as response to stress, personality for adaptation, family response and demands of a chronic metabolic disease.

There is a relationship between emotionally stressful experience and metabolic control in diabetes. Blood glucose fluctuates widely up or down under emotionally upsetting conditions. Stress may even herald the onset of ketosis and often accounts for metabolic instability in a diabetic. Adaptation behaviour is variable; personal attitude of coping with a situation determines whether or not the individual is dependent on others in day to day care or is independent. Responsible self care, regularity and compliance to treatment also depend on one's personality. Family response can be variable for example non-acceptance leads to discord, denial and anxiety or depression. On the other hand there can be overindulgence, empathy and overdone responsibility for the care of the diabetic. There is no evidence per se for increase in psychiatric disturbances among diabetics.

Psychological response is variable-denial to minimize the handicap, or due to poor self perception, greater anxiety, cognitive dysfunction and difficulties in achieving sexual identity.

Malnutrition related Diabetes (V. C. Mathew Roy)

In tropical countries 6-7% of diabetes is due to chronic pancreatitis. The presentation can be (i) diabetes mellitus, pain, pancreatic calculi 50% (ii) diabetes mellitus, pain, no calculi 25 %, (iii) diabetes mellitus, no pain, calculi 20 % (iv) no diabetes, pain, calculi 6.4%.

The common age group is 15-35 years, males are three times more often affected than females, there is familial history in 10%, and 80% of the cases come from very low socio-economic group.

Pancreatic biopsy has shown complete atrophy in 9.4%, regeneration in 25%, inflammation in 21 %, and fibrosis in 42.0%. Autopsy data (18 cases) has shown fatty lesion in 7, cirrhosis in 2, atheroma in 5 and pulmonary tuberculosis in 7, hypoglycaemia 2.

Surgical aspects of diabetic foot (L.K. Sharma)

Statistics in Western world show that peripheral vascular disease occurs in 30% of diabetics, and 7% of the hospitalized diabetics need amputation or a surgical procedure on the foot.

Pathogenesis of arterial disease from the stage of endothelial injury, platelet aggregation, plaque formation and complicated lesion of atherothrombosis was elaborated. Grading of peripheral vessel involvement was stated as follows :

G-0	G-I	G-II	G-III	G-IV	G-V
No superficial ulcer	Superficial ulcer	Deep ulcer	Abscess, osteitis	Gangrene part of foot	Gangrene entire foot

In management of the diabetic foot, local cleansing with weak hydrogen peroxide solution, daily debridement, and wide incision and drainage were advised. The role of non-invasive techniques such as Doppler ultrasonography in studying peripheral vascular disease was exemplified as was the role of percutaneous catheter angioplasty in selected cases.

The Doppler findings were collaborated with angiography. (M. Sheikh)

Finding on ultrasound (US)

US pattern		Angiography pattern	
		Normal	Abnormal
Triphasic	80	93.6%	6.4%
Biphasic	55	--	100.0%
Non-specific	8	87.5	12.5%

Peripheral vascular disease in diabetes is diffuse, bilateral and shows irregular skipped lesions, while in non-diabetic it is localized and single segmental.

CLINICAL CONFERENCES

Clinical presentations included a clinicopathological conference (CPC), radiological conference, therapeutic conference, patient management problems and nutritional counselling conference.

In the CPC, (S.S. Rastogi, U.N. Bhuyan) clinical history of the patient was as follows: a female aged 25 years age had IDDM for 6 years and was receiving 40-50 U of insulin per day. She had hypertension, retinopathy and albuminuria, there had been ankle swelling and erythematous rash on the lower extremities two years ago. Blood pressure 160/100 mm Hg. On investigation, she had albuminuria (+ to ++) 2-4 WBC/HPF, urea and creatinine were in the normal range. Antinuclear factor was positive and so were TMA and PCA. A renal biopsy had been performed at this stage. In 2 years follow up the clinical status had not shown much deterioration, she continued to have hypertension, retinopathy, albuminuria. Renal function showed adequate compensation. Discussion was centered around the nature of the renal pathology in the case. The differential diagnosis was diabetic glomerulosclerosis, immune complex glomerulopathy, vascular collagen disease (SLE), or primary renal disease (proliferative or membranous glomerulonephritis). Relatively long duration of diabetes, absence of systemic stigmata of autoimmune disease, and the good renal function status at present excluded some of the above conditions. Histological features showed diffuse involvement of glomeruli, proliferation of mesangial cells and narrowing of arteriolar lumen (no microangiopathy). Immune complexes were deposited linearly and basement membrane thickening showed a splitting pattern (not uniform thickening). The final diagnosis was mesangioproliferative glomerulopathy in IDDM.

In the therapeutic conference, (H.B. Chandalia, G.R. Sridhar,) three problem cases were presented where the choice of specific therapeutic agent was to be discussed in the context of its usage in a diabetic with associated complications.

A middle aged male with NIDDM was being administered chlorpropamide. He had hypertension which was not controlled despite the use of chlorothiazide, propranolol and prazosin. He was already having postural hypotension, low serum K⁺ and multiple ventricular ectopic beats. The side effects were related to the present drug regime. Discussion of side effects of chlorpropamide (water retention), chlorothiazide (low K⁺, ventricular ectopics) and combination of chlorothiazide and propranolol (postural hypotension) were explained. Replacement of K⁺ would be required immediately, and in the present situation, use of spironolactone as a diuretic and captopril for the control of hypertension was advised.

In the second case a 32 year old male diabetic, incapacitated due to muscular dystrophy and immobilized in a wheel chair was admitted with injection abscess. Weight was 65 Kg. and height 156 cms. He was receiving 360 units of insulin per day (40 units of regular and 80 units of NPH insulin before breakfast, 120 units of regular insulin before lunch and also before dinner). Discussion centred around the choice of therapy in non-insulin dependent diabetes in the young. It was felt that such overweight individuals are usually overinsulinized and the higher insulin requirement here was due to 'pseudoresistance'. It was advised to gradually reduce the insulin, introducing some NPH insulin replacing regular insulin at dinner and later seeking if oral sulphonylureas would not stabilize the glycaemia in this case. In an ideal setting, C-peptide estimation (basal and following administration of sulphonylureas) would provide a scientific rationale for this change.

The third case was a 52 year old female stabilized on metformin. She was also taking phenytoin for grand-mal epilepsy. She was found to have a pulmonary parenchymal lesion (pulmonary tuberculosis) and was receiving isoniazid, rifamycin and ethambutol. She now presented with a hyperosmolar state. In the discussion, the hyperosmolar state was related to the use of phenytoin. Other risks associated with metformin such as lactic acidosis were also discussed.

Reference to the use of anti-tuberculous drugs, acetylation and glycosylated hepatic excretion of drugs was to be borne in mind. After evaluation of the hepatic enzyme status, antituberculous drug dosage and frequency can be guided. INH must be administered in lower dosage in patients with diabetes due to slow acetylation.

Case Demonstrations

In patients management problems (V. Seshiah, A. Mithal) three patients with different aspects of diabetes and complications were highlighted. The first case was a 32 year old female with IDDM and the following clinical presentation :

1. Recent facial palsy (LMN) type, polypoid mass in the middle ear and evidence of diabetic peripheral neuropathy.

2. Generalized anasarca, with hepatomegaly and raised JVP.
3. Cutaneous macular lesions on the trunk and lower extremities.
4. Retinopathy, proliferative type causing blindness.
5. Nephropathy as evidenced by albuminuria, rising blood urea and creatinine.

Biopsy of the polypoid mass in the ear showed chronic inflammatory granulomatous tissue. Mucormycosis was excluded by culture. Echocardiography indicated evolving stages of constrictive pericarditis. Tuberculosis in diabetes need not always be of exudative nature. Skin biopsy showed changes of diabetic dermatopathy. Other microvascular complications did not seem duration related in this case.

The second case was an uncontrolled diabetic with a carbuncle. Insulin even in very high dosage >380 U/24 hr by the subcutaneous route did not bring about adequate glycaemic stabilization. I.V. insulin in pump and monocomponent insulin were effective, however. Possible rapid tissue degradation of insulin or the presence of insulin antibodies were considered responsible for this status.

The third case was a 36 year old male who had received insulin for 3 years to achieve control of the hyperglycemic state. At present he was however not requiring any insulin. Blood glucose was normal indicating a complete remission of diabetes. Mode of present management with diet was discussed. Evaluation of islet cell antibodies, size of pancreas by ultrasound and HLA typing would further elucidate prospects of recurrence of diabetes in this case.

In the *nutritional planning conference (Rekha Sharma)*, case discussions included :

- a) NIDDM case with bleeding duodenal ulcer, coronary insufficiency. Problems relating to IV alimentation and provision of basal calories with coverage by regular insulin therapy was discussed. In ambulatory phase, role of bland diet, polyunsaturated fats and return to OHA was discussed.
- b) Hepatitis in an IDDM, having background retinopathy and nephropathy-specific nutritional problems related to hepatitis, easy tendency to hypoglycemia and the need for increase in carbohydrates was discussed. For insulin pump therapy schedule of distribution of 3 meals, 2 snacks and proportionate carbohydrate CH₂O 60%, fat 20-25%, protein 10-25% was discussed (45 calories per Kg were permitted and 1 unit of insulin covered about 15 g of carbohydrate).
- c) The third case was a twin pregnancy in an NIDDM. The recommendations were to use two or three doses of insulin per day providing 30 Cal/Kg body weight. Strict glycaemic control by regular monitoring and allowing no excessive weight gain during pregnancy (twin pregnancies were not considered additional risk in a diabetic) were the recommendations while carefully monitoring fetal development and growth by ultrasound.