पल्स Pulse

खंड 11
Volume 11

अगस्त 2009
August 2009

Homi Bhabha Birth Centenary Year
30 October 2008 - 30 October 2009

THE INDEPENDENT

NEWSPAPER OF THE YEAR

Today education & careers

World health body raises alarm over modern-day disease

Diabetes: health crisis of the 21st century

£4bn

1.8m people in the UK have diabetes - a

37"

The UK

31.5"

The world

10% When six years ago one person in every 20 spent on the NHS will go on treating diabetes

450% rise on 1996

30

41,000

100,000 people in the UK are diagnosed with Type 2 diabetes - which is linked to obesity - each year

3m will be confirmed suffering within six years - an increase of 67% on today's figure

1-in-6

50% More than 50% of British children could be obese by 2020, according to the Royal College of Physicians

1m more are estimated to have diabetes - but don't even know it

1/2

80%

अंशदायी स्वास्थ्य सेवा स्कीम
CONTRIBUTORY HEALTH SERVICES SCHEME

सत्यमेव जयते

भारत सरकार
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BHABHA ATOMIC RESEARCH CENTRE
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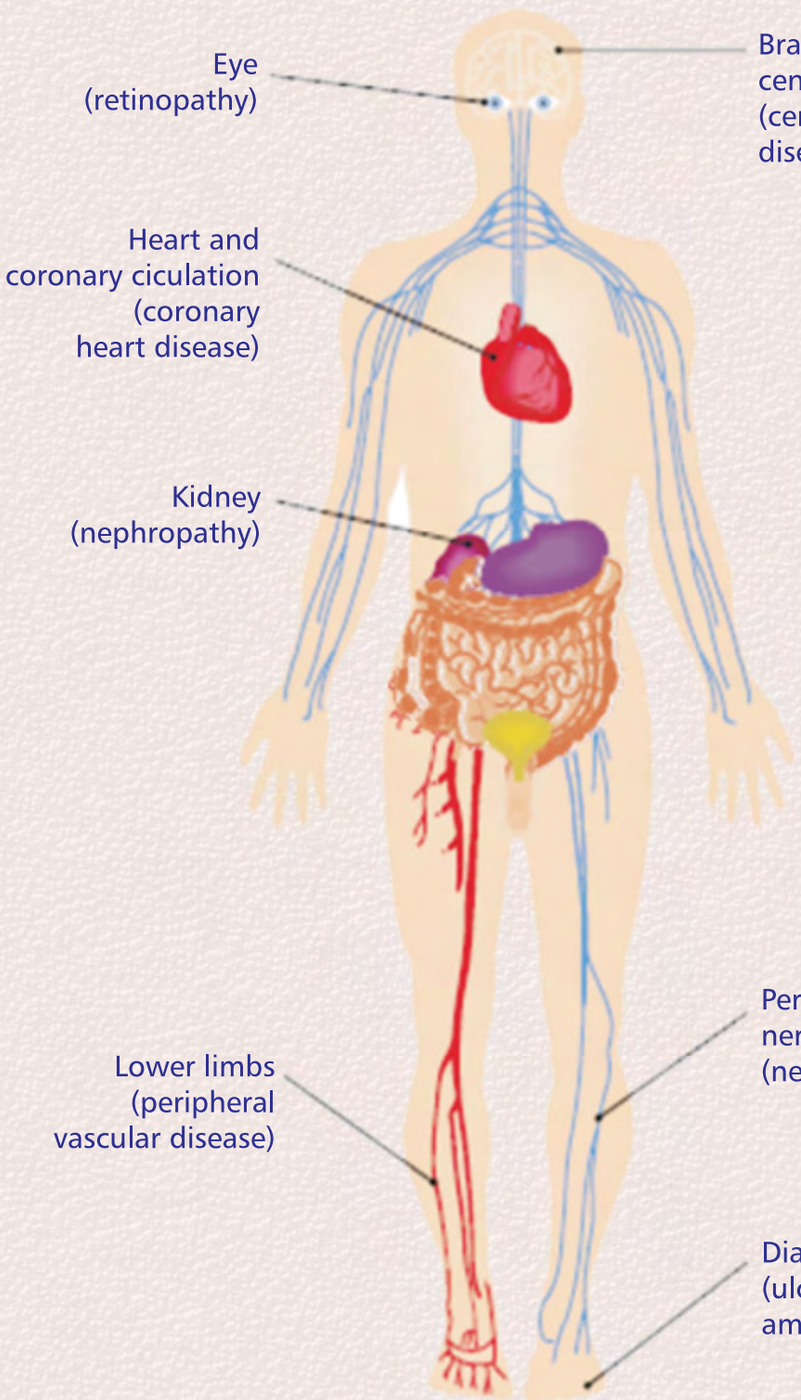
Anushaktinagar, Mumbai - 400 094.

The major diabetic complications



पल्स Pulse

BARC HOSPITAL NEWSLETTER

खंड 11 अगस्त 2009
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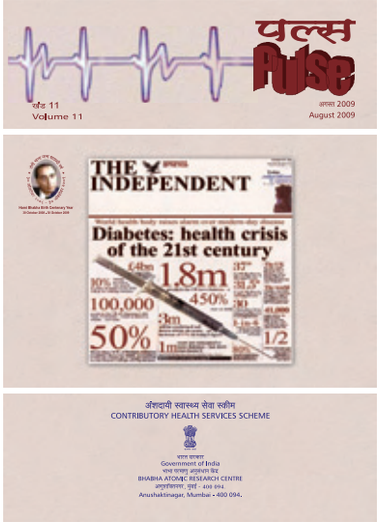

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Author guidelines for contribution to PULSE

It is essential to uniformly follow, as far as possible, a format for the submitted articles, which is broadly enumerated below:

1. Choice of topic / title to be governed by its relevance to the Medical Division's scope of work.
2. The importance / critical application of the subject.
3. Historical background (In brief).
4. Theoretical aspect (In brief) to facilitate understanding.
5. Present status with respect to Medical Division.
6. Interface with other disciplines, if any.
7. Specific contribution by the unit.
8. Enhancement / upgradation / future plans.
9. Conclusion.
10. References.

Case reports of practical interest to clinicians are also invited for publication.

Articles should be sent as Microsoft Word documents in both hard as well as soft copy to:

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CMEs Conducted at BARC Hospital

DATE	DEPARTMENT	TOPIC
09.01.2009	ORTHOPEDICS	Advances In Management of Osteoporosis – Our Experience
15.01.2009	ENT	Tracheostomy
23.01.2009	ANAESTHESIA	Pre-Anaesthetic Evaluation of Patient With Cardiac Diseases For Non Cardiac Surgery
13.02.2009	PSYCHIATRY	Addiction Newer Approach
27.02.2009	PATHOLOGY	Pre-Analytic Factors Affecting Quality Control In Pathology Laboratory
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26.06.2009	GYNAECOLOGY	Conservative Management of Ectopic Pregnancy

"The diabetes time bomb had been ticking for 50 years. Despite the warning, successive generations of world leaders have largely ignored the threat. Diabetes has now exploded with the force felt greatest in the Middle East India, China and the USA."

Martin Silink
President
International Diabetic Federation

Diabetes affects 5.9% of the world adult population. There has been steady increase in the incidence of diabetes in the current decade. This has prompted us to choose the disease as the topic of this issue. Lifestyle changes, stressful life along with the genetic predisposition are primarily responsible for the increasing incidence of this condition.

Diabetes mellitus (DM) a group of metabolic diseases can be classified into four clinical classes – Type 1 accounting for less than 10% cases of DM, type 2 accounting for more than 90% of cases, gestational diabetes complicating 4% of all pregnancies and other specific types of DM which include those resulting from genetic defects of insulin secretion or action or exocrine causes.

In this issue, in an article on "Diabetes mellitus in childhood and adolescence" the natural history of type 1 diabetes has been illustrated in detail. It is interesting to know that in absence of islet autoantibodies insulitis is silent and only minority of genetically susceptible individuals develop islet autoantibodies and eventual Type 1 DM. Comprehensive approach is necessary for the successful management of DM. A team approach that includes the expertise of diabetes educators, dieticians and other members of diabetes care team offers the best chances of success in management. Prevention of long term complications is one of the main goals of diabetes management. Appropriate treatment of established complications may delay their progression and improve quality of life. Microvascular complications include diabetic retinopathy, nephropathy and neuropathy. These complications can be prevented by tight glycemic control.

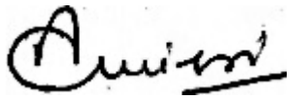
Current goals for Type 2 DM in Adults:

- *Hb A1C less than 7%*
- *Fasting Plasma Glucose 5.0 -7.2 mmol/l*
- *Peak Post Prandial Glucose less than 10 mmol/l*

The gestational diabetes usually resolves after delivery, although affected women remain at an increased risk for development of Type 2 DM in later life. These women should be evaluated annually for the onset of diabetes.

The management of DM in the geriatric population is a challenging task in view of various factors like difficulty in modifying lifestyle risk factors, co-existence of conditions, risk of adverse drug reactions, rapid development of complications and limited mental and physical abilities.

Good news – "The new incretin based therapies provide an option that might delay or avoid use of insulin a little while longer in those cases, who are fearful about injections", mentioned in the Guest Article by Dr. Poornima Jayaramaiah and Dr. Romesh khardori.



(Dr. Amrita Misri)

TYPES OF INSULIN

There are many types of insulin available today. They are classified by how they work in the body. It is important to know the ONSET, PEAK and DURATION of the insulin you take.

- Onset – how long it takes for the insulin to start working·
- Peak – this is when the insulin is working at its hardest·
- Duration – the length of time the insulin works

Insulin Name	Onset	Peak Effect	Duration
Rapid-Acting Insulins			
Lispro Humalog®	5-15 minutes	30-75 minutes	2-3 hours
Aspart Novolog®	10-20 minutes	1-3 hours	3-5 hours
Short-Acting Insulin			
Regular (R)	30 minutes	2-5 hours	5-8 hours
Intermediate-Acting Insulin			
NPH (N)	1-3 hours	6-12 hours	16-24 hours
Lente (L)	1-3 hours	6-12 hours	16-24 hours
Long-Acting Insulin			
Ultralente (U)	3-5 hours	8-14 hours	18 hours
Very Long-Acting Insulin			
Glargine Lantus®*	1 hour	Evenly for 24 hours	24-28 hours
Premixed Insulins			
NPH and Regular insulin mixed together in one of the following combinations. 70/30 or 50/50	30-60 minutes	2-12 hours	up to 18 hours

*Lantus should not be mixed in a syringe with any other form of insulin before use.

ORAL HYPOGLYCAEMIC AGENTS

	Type	Daily dose (mg)	Frequency of daily administration	Duration of action (hrs)
A.	Insulin secretagogue			
	1. Sulfonylureas			
	a. 1st generation			
	Chlorpropamide	100-500	1	60
	Tolbutamide	500-2500	2-3	6-12
	b. 2nd generation			
	Glibenclamide	2.5-20	1-2	12-24
	Glipizide	2.5-30	1-2	12-24
	Glipizide*L	5-20	1	24
	Gliclazide	80-320	1-2	12-18
	Gliclazide MR	30-120	1	24
	Glimipiride	1-8	1	16-24
	2. Meglitinide analogue			
	Repaglinide	1.5-10	3	2-4
B.	Insulin sensitisers			
	Biguanides			
	a. Metformin	250-2500	2-3	8-12
	b. Phenformin	50-150	3-4	6-8
C.	Alpha glucosidase inhibitor			
	Acarbose	25-200	3	4
D.	Insulin sensitisers			
	Thiazolidinediones			
	a. Rosiglitazone	2-8	1-2	12-24
	b. Pioglitazone	15-45	1	24

Newer Treatments for Type-2 Diabetes Mellitus

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Introduction:

Management of diabetes has undergone a sea of change in last 14 years since Metformin was reintroduced in medical management of those with type-2 diabetes. Most physicians have become comfortable with using medications targeting hyperglycemia and these include second generation sulfonylurea *(Glyburide, Glipizide, Glimepiride, Gliclazide)*, meglitinides *(Repaglinide, Nateglinide)*; thiazolidinediones *(Rosiglitazone, Pioglitazone)*; alphaglucosidase inhibitors *(Acarbose, Miglitol)* and biguanide *(Metformin)*. A clear understanding of the mechanism of action guides clinician's choices. Apart from these drugs other options include Pramlintide *(Symlin)*, and Colesevelam *(Welchol).* However, a new emerging class deserves attention. One of the drugs in this category (Exenatide /*Byetta*) has been in use for at least three years and the results have been gratifying. This category is often referred to as incretins. We shall be limiting discussion to this new category with the hope that it will provide a better appreciation of how these drugs work and how they could be used.

Pathophysiology of Type-2 Diabetes Mellitus:

In Type 2 Diabetes Mellitus, the secretion and action of insulin are impaired as opposed to type 1 diabetes in which there is absolute deficiency of insulin. The two major defects in type 2 diabetes are:

a) Impaired beta cell secretory function ([1]) and

b) Insulin resistance leading to increased hepatic glucose production and decreased peripheral glucose disposal.

Insulin resistance in hepatic and peripheral tissues, particularly in the skeletal muscle, leads to unrestrained hepatic glucose production and decreased insulin stimulated peripheral glucose utilization ([2]). Normal blood glucose is maintained in the initial stages as the increased insulin secretion compensates for the insulin resistance. In patients who develop type2 diabetes insulin secretion eventually fails and leads to hyperglycemia and diabetes ([3]). The difficulty in maintaining the stable glycemic status over time may be related to several behavioral factors (for example unhealthy eating, medication regimens and exercise) but primarily reflects the decline in beta cell function ([4]).

Type 2 diabetes has been treated traditionally in a stepwise manner with lifestyle changes ([5-7]), exercise ([8]) and later on pharmacotherapy with oral agents. Pharmacotherapy mainly includes insulin secretagogues and insulin sensitizers. Over time, many patients with type 2 diabetes will eventually require insulin therapy ([9-11]). The new incretin based therapies provide an additional option that might delay or avoid use of insulin a little while longer in those fearful of injections.

Incretin Effect

In his "Lessons on diabetes" ([12]) published in 1877 Claude Bernard, the French investigator recorded that larger amounts of glucose can be given orally rather than intravenously without production of glucosuria. In 1906 Moore et al ([13]) in Liverpool, England proposed that duodenum supplies a chemical excitant for internal secretion of pancreas and that in patients with diabetes increased urine glucose might be due to the absence of such an intestinal excitant. The term incretin was introduced by LaBarre from Belgium in 1932 ([14]). Due to the negative results of Loew et al. the incretins were relatively abandoned ([14a]). In mid 1960s when several groups demonstrated the incretin effect the interest in this area was revived ([14b]). Enteroinsular axis was the term given to the connection between the gut and the pancreas by Unger ([14c]) in 1969. Ten years later, Creutzfeldt ([14d]) defined incretin as a gut-derived endocrine transmitter, released by nutrients that stimulates pancreatic insulin secretion in the presence of glucose.

For an agent to be called as incretin the following criteria must be fulfilled.

1) It must be released in response to oral nutrient ingestion especially glucose and

2) it must reach physiologic concentrations in vivo to cause insulin release.

Glucagon-like peptide-1 (GLP-1), and glucose dependent insulinotropic polypeptide (GIP) are currently the only known incretins. The incretin effect is the augmentation of glucose-stimulated insulin secretion by intestinally derived peptides, which are released in the presence of glucose or nutrients in the gut. GLP-1 and GIP are the incretins which are enteroendocrine hormones released into bloodstream from the K and L cells in gut in response to ingested nutrients. They provide additional stimulus to insulin secretion during oral ingestion that is not present with IV glucose infusion ([15, 16]). In newly diagnosed type 2 diabetes mellitus patients who have relatively good control with a glycated hemoglobin (HbA1c) of about 6.9% the GLP-1 and the GIP secretion in response to mixed meal challenges and glucose are same or even increased when compared with healthy subjects ([17,18]). In long standing type 2 diabetes patients with poor control with an HbA1C of about 8-9% GLP-1 response is decreased while GIP secretion is unchanged ([19-20]). Acute GLP-1 administration increases the insulin secretion to normal levels and lowers plasma glucose effectively ([21,22]) as opposed to the GIP which has markedly reduced insulin tropic actions with little or no glucose lowering effects in type 2 diabetes ([22-23]). Therefore treatment for type 2 diabetes within the incretin field is focused on use ofGLP-1, GLP-1 receptor agonists, GLP-1 analogs or GLP-1 mimetic.

Non-insulinotropic effects of GLP-1 in treatment of type-2 diabetes:

Incretins cause suppression of glucagon secretion in the presence of hyperglycemia and euglycemia, leading to improvement in glycemic control and hepatic insulin resistance ([24, 25]). Higher the glucose levels higher the effect of GLP-1, and little or no effect when the plasma glucose concentration is low. Delaying the gastric emptying and gut motility causing decrease in postprandial glucose excursion ([26]); help with weight loss, decreased food intake and improved insulin resistance by increasing postprandial satiety ([27-29]). Continuous subcutaneous GLP-1 infusion via a pump for 6–12 wk improved insulin pulse mass and pulsatile insulin secretion, enhanced insulin-mediated glucose disposal, glucose-induced insulin secretion ([30, 31]). Intravenous GLP-1 infusions overnight markedly improved cell function, lowered fasting plasma glucose (FPG) and post prandial glucose (PPG) to near-normal

levels and restored first-phase insulin secretion, the absence of which is a hallmark of type 2 diabetes ([32]). Subcutaneous administration of GLP-1 as a bolus before breakfast, lunch, and dinner for 7 days improved PPG and decreased plasma lipid levels significantly ([33]). Beta cell failure is one of the fundamental defects of type 2 diabetes, recent animal studies have shown that exogenous GLP-1 has the ability to enhance -cell proliferation, increase islet size, regulate islet growth and inhibit cell apoptosis ([34, 35]).

Physiology of GLP-1

GLP-1 is a product of the glucagon gene, which is expressed both in pancreatic alpha cells and Intestinal endocrine cells called L cells, located mostly in the lower small intestine and colon. Proglucagon is cleaved primarily to glucagon in alpha cells and to GLP-1 in L cells. Once GLP-1 is released from the L cells it is rapidly degraded by serine protease, dipeptidyl peptidase 1V (DPP-1V) which cleaves the N - terminal dipeptides from GLP-1 and renders it inactive ([36, 37]). In addition to this GLP-1 is hydrolyzed at six different places by neural endopeptidase ([38]). GLP-1 receptor is expressed in pancreatic beta and alpha cells, vagal afferent nerves, heart, lung, stomach, kidney and specific brain areas. Circulating GIP and GLP-1 concentrations rise 15 minutes after ingestion of food peaks by 30-45 minutes and returns to basal values by 2-3 hrs.

GLP-1 Agents in treatment of Diabetes Mellitus:

GLP-1 has a very short half- life and has to be administered by continuous or frequent injections. Two options for GLP-1-based therapies are GLP-1 mimetic resistant to enzymatic degradation (DPP-IV) to achieve a longer half-life or agents such as DPP-IV inhibitors, which increase plasma endogenous GLP-1 levels.

GLP-1 Mimetics

GLP-1 mimetic circumvents the problem of rapid metabolism by DPP-IV. DPP- IV cleaves peptides with an alanine, proline, or hydroxyproline in the penultimate N-terminal position. Various modifications of GLP-1 at His7, Ala8 or Glu9 have been investigated ([39]). Additional mid-chain modifications of GLP-1 to prevent neutral endopeptidase (NEP) hydrolysis are also being investigated to provide longer plasma half-life. Exenatide and liraglutide are two compounds that exhibit these characteristics.

Exenatide (Byetta): Synthetic exendin-4 is a 39-amino acid peptide produced in the salivary glands of the Gila monster lizard (Heloderma suspectum) with 53% amino acid homology to full-length GLP-1 and is a potent GLP-1 receptor agonist. Exendin-4 is not a substrate for DPP-IV because it has a Gly8 in place of an Ala8. In addition, it lacks some of the target bonds for NEP and its secondary and tertiary structures may also prevent NEP hydrolysis. Exenatide being a peptide, must be injected sc and is eliminated by the kidneys through glomerular filtration ([40]). It has a mean half-life of 3.3–4 h, is still detected in the plasma 15 h after sc injection, and has biological effect 8 h after dosing ([41]).

Exenatide is injected subcutaneously twice daily before two major meals of the day and the two doses should be at least 6 hrs apart. The recommended initial dosing is 5 micrograms twice a day and can be increased to 10 micrograms twice a day to achieve glycemic goals. It is available in prefilled syringes that hold a month's supply of either 5 or 10 mcg doses. When administered with sulfonylurea's there may be a dramatic increase in insulin secretion at levels below which insulin secretion is not stimulated thereby increasing the risk of hypoglycemia([42]). Exenatide is currently not approved for use with insulin.

As a monotherapy for type-2 diabetic patients, exenatide 5 micrograms twice daily for 4 weeks followed by 10 micrograms for 20 weeks resulted in a A1C drop of 0.9% and fasting plasma glucose of 18 mg/dl compared to 0.2% (P 0.0004) and 5 mg/dl (P0.016) for placebo respectively ([43]). Bodyweight decreased 3.1kg with exenatide and 1.4kg with placebo (P 0.003).

With exenatide 10 microgram twice daily as adjuvant therapy to oral hypoglycemic agents, a significant number of patients (32–62%) achieved HbA1c of 7% or less when compared with placebo (7–13%), glargine (48%), and biphasic insulin aspart (24%) and HbA_{1c} reductions of 0.8–1.1% were sustained up to 3 yr. Progressive weight loss from 1.6 –2.8 kg noted at 30 wk to 5.3 kg at 3 yr was also noted ([44–49]). Exenatide showed better reduction of postprandial glucose than fasting glucose, while glargine showed a better reduction in fasting glucose. HbA_{1C} levels after 6 months in both groups were comparably reduced. Weight increased approximately 1 kg in glargine group, while weight was reduced by more than 2 kg in those who received exenatide ([49a]).

Side effects: Nausea and vomiting are the most common side effects of exenatide. Nausea was mild to moderate and decreased about 8 weeks after treatment. When prescribed with sulphonylureas the dose of sulphonylueas should be reduced as it can cause hypoglycemia. Cases of acute pancreatitis have been reported since the release of exenatide in 2005 ([50]). There have been 36 reports of acute pancreatitis in patients taking exenatide. In some cases hemorrhagic or necrotizing pancreatitis was reported. The overall reporting rate for pancreatitis in exenatide users is 1 in 3000 and for the more severe necrotizing or hemorrhagic forms, less than 1 in 10,000, which is similar to the background rate in patients with diabetes mellitus. In any patient who is complaining of severe abdominal pain with or without nausea, pancreatitis should be considered and exenatide should be discontinued.

Long acting GLP-1 agents

Exenatide LAR is a sustained release formulation of exenatide with a median half life of two weeks. Forty-five patients with type 2 diabetes who were inadequately controlled with metformin and/or diet and exercise were given exenatide LAR (0.8 or 2 mg) subcutaneously once a week for 15 weeks and the mean A1C was reduced by -1.4 and -1.7 in 0.8 and 2 mg groups compared to 0.4 % increase in the placebo group ([51]). Another noninferiority trial of exenatide LAR (2mg) versus twice a day dosing of 10 mcg showed similar glycemic outcomes ([52]). Nausea which is the most frequent adverse effect was reported less frequently with LAR than twice daily formulations. It is not currently available for clinical use.

Liraglutide is long acting GLP-1 analog which is modified to non-covalently bind to albumin by a lipid side chain resulting in slow absorption from subcutaneous injection site and a longer plasma half life. It has an elimination half life of 12 hrs after the subcutaneous dose. 190 patients with type 2 diabetes were randomized to receive liraglutide in one of five doses, glimeperide for 12 weeks or placebo. The absolute reduction of A1C was 0.8 % and the glucose lowering effect was comparable in the highest dose liraglutide (0.75 mg) and glimepiride group ([53]). In patients with type 2 diabetes, one dose of liraglutide at bedtime decreased the fasting and the postprandial glucose values as a result of suppressed glucagon release, enhanced insulin secretion and delayed gastric emptying ([54]). Most frequently reported adverse effect was nausea and vomiting. The federal drug agency (FDA) has not yet approved this drug for clinical use.

DPP –IV Inhibitors (The Gliptins):

These agents enhance endogenous incretin effect by blocking the degradation of the GLP-1 and GIP. DPP 1V is a member of a family of serine peptidases and functions both as a protein and as an enzyme involved in many processes throughout the body related to nutrition, immune function and excretion ([55]). The enzyme is found on the surface of endothelial cells and is also circulates in soluble form allowing close contact with the circulating hormones ([56]). In addition to the incretin peptides, DPP-IV has many other peptide substrates, including neuropeptide Y, peptide YY, and substance P, pituitary adenylate cyclase activating peptide (PACAP), and growth hormone–releasing hormone. Many of these peptides maintain at least some biological activity after cleavage by DPP-IV in contrast to GLP-1 and GIP ([55]).

In animal studies, DPP-IV knockout mice have improved glucose tolerance and enhanced insulin secretion ([57]). Human studies show enhanced postprandial insulin secretion and reduced glucose rise in response to treatment with DPP-IV inhibitors ([58, 59]). In addition DPP-IV inhibitors also lower postprandial glucagon and endogenous glucose production. Unlike GLP-1 mimetics, DPP-IV inhibitors do not appear to alter gastric motility ([59, 60]).

Interestingly, treatment with DPP-IV inhibitors does not increase the total GLP-1 level but the ratio of active to inactive GLP-1 level is increased ([61,62]). DPP 1V inhibitors do not delay gastric emptying which may explain the lack of gastrointestinal side effects seen with GLP-1 mimetics ([63,64]). Sitagliptin and Vildagliptin are the DPP1V inhibitors.

Sitagliptin (Januvia): Sitagliptin is an orally active, selective inhibitor of DPP1V. It is rapidly absorbed reaching a peak plasma level in 1-6 hrs, with a half life of 8-14 hrs. The pharmacokinetic profile is not changed when it is taken with food and majority of the drug is excreted unchanged in the urine ([65, 66]). Sitagliptin 100mg achieves over 80% inhibition of DPP1V activity over 24 hr period ([65]). A dose has to be reduced to 50 mg if the creatinine clearance is less than 50ml/min and to 25 mg if creatinine clearance is less than 30 ml/min ([67]).The treatment effect of sitagliptin on HbA1c value has been considered modest, it is highly dependent on the baseline HbA1c value and has been reported to be as effective as sulfonylurea's ([68]).

Sitagliptin / Metformin combination therapy as an initial treatment worked better than sitagliptin or metformin monotherapy with an HbA1c reduction of 1.9% compared to 0.6-0.6% and 1.13% after 24 weeks ([69-73]). As an adjuvant therapy sitagliptin with glipizide, pioglitazone or metformin reduced the HbA1c by 0.6-0.7% when compared with placebo. In a 52 week trial on glipizide Vs sitagliptin as adjuvant therapy to metforin showed a reduction in HbA1c of 0.7% in both groups and the maximum HbA1c reduction was observed at 24-30 weeks with a slow increase in HbA1c from week 30-52, which raises the issue of declining sitagliptin efficacy ([74]).

Side effects: Sitagliptin monotherapy or combination therapy was well tolerated and hypoglycemia occurred in the setting of combination therapy ([75]). The side effects that were higher with sitagliptin compared with the nonexposed groups were contact dermatitis, nasopharyngitis and osteoarthritis.

Vildagliptin: It is an orally administered, stable, highly potent selective inhibitor of DPP 1V ([76]). It is rapidly absorbed and reaches a peak plasma level in 1-2 hrs. It has a shorter half life than sitagliptin which is 2 hrs ([77-78]). It has a bioavailability of 85% and its pharmacokinetics is not affected by food ([79-80]). 85% of vildagliptin is metabolized by hydrolysis in the liver to LAY

151, which is inactive. The remaining 15% is eliminated unexchanged in the kidneys ([81]). FDA requested additional data on patients with renal impairment before granting final approval of vildagliptin. Vildagliptin 50mg twice a day as a monotherapy was as effective as acarbose 100 mg three times a day and rosiglitazone 8 mg once a day in decreasing HbA1c but not as effective as metformin 1000 mg once a day ([82-84]). Patients with higher HbA1c (8.4 vs. 6.7%) had a bigger reduction in HbA1c over24 weeks and data on extension study on the group with better glycemic control showed that HbA1c reduction was maximum at 24-30 weeks and was followed by a gradual increase thereafter until week 108 ([85]). As an adjuvant therapy vildagliptin administered to patients with poor glycemic control on metformin, sulfonylurea, thiazolidinedione or insulin therapy resulted in further HbA1c reductions of 0.6, 0.9, 1.0, and 0.5% respectively ([86-89]). The side effects of viladagliptin are comparable to that of sitagliptin.

Summary:

New class of drugs – incretins offer another modality of treatment in patients with diabetes mellitus. A clear understanding of the incretin concept should facilitate understanding of how these drugs could be used in day to day management of patients routinely seen in clinics. These drugs are new and hence caution is advised in their in unrestrained use since long term effects of these therapies are not available. Exercise of prudence is advised.

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Diabetes care: 10 ways to avoid complications

1. Have a General Physical Examination each year
2. Get a yearly eye examination
3. See your dentist twice a year
4. Keep your vaccinations up-to-date
5. Take care of your feet
6. Don’t smoke
7. Take a daily aspirin
8. Monitor your blood pressure
9. Monitor your blood sugar
10. Manage your stress

Diabetes Mellitus in Childhood and Adolescence

Dr. Santosh Kumar
Medical Officer
Department of Paediatrics

Introduction:

Diabetes mellitus (DM) is a metabolic syndrome characterized by chronic hyperglycemia and other metabolic disturbances, resulting from absolute or relative insulin deficiency. Besides asthma, diabetes mellitus is the most common chronic illness of childhood.

History of diabetes and insulin:

Diabetes has been recognized as a disease since ancient times – the word 'diabetes' coming from the Greek meaning 'to pass through'. It was first used by Aretaeus of Cappadocia in the 2nd century AD who described a serious condition involving the 'melting down of flesh and limbs into urine'. He went on to observe that 'life was short, unpleasant and painful, thirst unquenchable, drinking excessive and disproportionate to the large quantity of urine'. However, it was not until 1889 that diabetes began to gain significant interest from scientists and medical professionals when two German scientists, Oskar Minkowski (1858–1931) and Josef von Mering (1849–1908), discovered that when they removed the pancreas from a dog, it developed diabetes. They learnt from this that diabetes is related to a pancreatic disorder. The next major milestone in the history of diabetes came in 1921 with the discovery of insulin at the University of Toronto, Canada. Collaborative work between the surgeon Frederick G. Banting (1881–1941), one of his students Charles H. Best (1892–1965), James B. Collip (1892–1965) a biochemist, and the physiologist J.J.R. Macleod (1876–1935) found that chilling the extracts of dog pancreas and then injecting them into a dog with diabetes caused a decline in the dog's blood glucose level. From this discovery, Collip went on to develop improved procedures for the extraction and purification of insulin from pancreas, and on 1st January 1922 the first person with diabetes was treated with insulin – a 14-year-old boy called Leonard Thompson. Based on this discovery and the experiences of Leonard Thompson, the chemists Eli Lilly and Co. from USA jumped on to the commercial bandwagon. They worked out processes to refine insulin extraction and purification, resulting in insulin becoming commercially available in North America and Europe from 1923. The past 75 years have seen the development, redevelopment and marketing of different types of insulin, with varying peak onset and action times. The supply of insulin from cow and pig pancreas was shifted to new genetically modified analogue insulins introduced into the market in 1983. These new-generation insulins such as Humalog and more recently Novorapid have been produced via scientific technology that enables human insulin to be commercially produced from Escherichia coli bacteria using recombinant DNA or cloning. This brings us right up to date with the development of inhaled insulin Exubera.

Diagnostic criteria for diabetes:

1. Symptoms of diabetes plus casual plasma glucose concentration $\geq$ 200 mg/dl (Casual is defined as any time of day without regard to time since last meal.)

Or

2. Fasting plasma glucose $\geq$ 126 mg/dl (Fasting is defined as no caloric intake for at least 8 h.)

Or

3. Two-hour post-load glucose $\geq$ 200 mg/dl during an OGTT

The test should be performed as described by WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water or 1.75 g/kg of body weight to a maximum of 75 g.

Criteria for the diagnosis of DM were recently revised to include a new threshold for the diagnosis of impaired glucose tolerance (IGT) and impaired fasting glucose (IFG). IGT and IFG are 2 h plasma glucose between 140-200 mg/dl or a fasting glucose between 100-125 mg/dl respectively.

Type 1 Diabetes Mellitus:

Type 1 diabetes is a chronic autoimmune disease in which the T lymphocytes infiltrate the insulin-producing beta cells of the pancreas and progressively destroy them. By the time a person begins to develop the signs and symptoms of type 1 diabetes, over 90% of their beta cells have been destroyed; this causing a marked insulin deficiency, which is the hallmark of type 1 diabetes.

Incidence:

Annual incidence varies from 0.61 cases per 100,000 population in China, to 41.4 cases per 100,000 population in Finland. Most countries report that incidence rates have at least doubled or more in the last 20 years. The regional data in India shows a prevalence of 0.7/1, 00,000 population in 0-19 years of age.

Etiological classification:

Type 1 diabetes mellitus

Type I A- Autoimmune

Type I B- Idiopathic

Type 2 diabetes mellitus

Other specific types of diabetes

Pancreatic disease - Cystic fibrosis, Fibrocalcific pancreatic diabetes

Endocrine disease- Cushing's, Thyrotoxicosis, Growth hormone excess

Drugs- Steroids, Pentamidine, Thiazides, Diazoxide

Infection- Congenital rubella

Genetic defect- Mutation in glucokinase and transcriptase gene(MODY), sulphonylurea receptor gene in neonatal dibetes.

Genetic defect in insulin action- Leprechaunism

Autoantibodies against insulin receptor and insulin

Genetic syndrome- Klinefelter, Turner, Wolfram, Prader-Willi syndromes.

Etiology and Pathogenesis:

Genetic Predisposition - Clear evidence suggests a genetic component in type 1 diabetes mellitus. HLA class II molecule (DR and DQ) have strongest association with T1DM. HLA-DR3/DQ2 or DR4/DQ 8 increases susceptibility to T1DM. These high risk alleles are present in more than 90% of patients with T1DM. Resistance to T1DM is associated with the alleles DR15/DQ6. This allele is present in only 3% of children with T1DM. HLA associations in T1DM population in India showed strong association with DR3/DQ2.

Environment - Viral infections may be the most important environmental factor in the development of type 1 diabetes mellitus, probably by initiating or modifying an autoimmune process. Instances have been reported of a direct toxic effect of infection in congenital rubella.

Dietary factors - Breastfed infants have a lower risk for insulin-dependent diabetes mellitus (IDDM), and a direct relationship is observed between per capita cow's milk consumption and the incidence of diabetes.

Intiation of autoimmunity and pre-diabetic phase:

Immune response starts initially against foreign antigen (Virus), leading to cytotoxic T cell attack aided by T helper cells that are activated by macrophages. If homology exists between viral protein and β cell surface protein, the T cell response may then be directed against β cell (Autoimmunity). With the initiation of autoimmune attack, various cytokines are liberated which amplify the immune response. These include interleukin 1 and 6, γ interferon and tumor necrosis factor α. Cytokines act by direct cell destruction, diminishing insulin secretion from the β cell and activating cytotoxic T cells.

A. Direct β cell injury: Autoantigens are presented by MHC class 1 molecule on the surface of beta cell are recognized by antigen specific CD8+ cytotoxic T cells.

B. Indirect(bystander) killing of β cell: Antigens presented to APC by MHC class ll molecule are recognized by CD4+ helper T lymphocytes, triggers the release of wide variety of cytokines (IFNα,TNFα, NO) resulting in apoptosis of nearby β cell.

Natural history of type 1 diabetes:

The natural history of Type 1 diabetes can be schematized into a number of stages. In Stage 1, where beta cell mass and function are normal; individuals who carry genetic

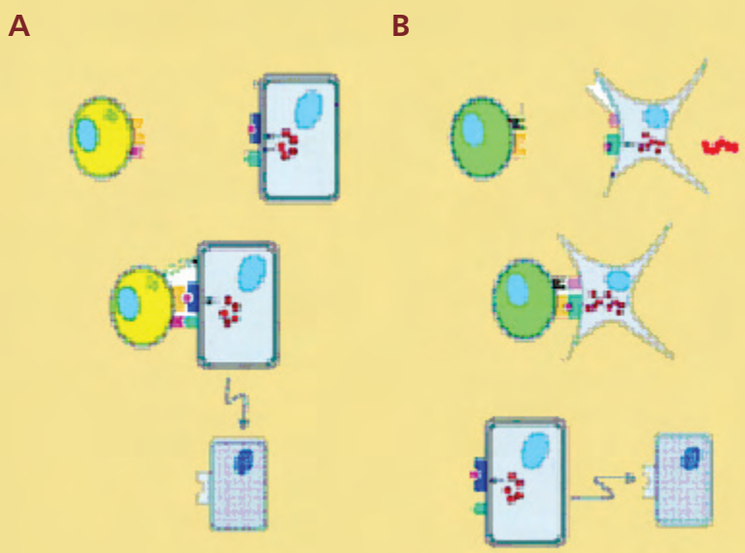


Fig: Mechanism of immune mediated killing of β cell

susceptible alleles to Type 1 diabetes suffer exposure to an environmental stimulus triggering islet inflammation (insulitis). The presumed release of sequestered or altered self-antigens explains, at least in part, the later development of islet autoantibodies that mark the recognition of Stage 2. In the absence of islet autoantibodies and any clinical evidence of beta cell dysfunction, insulitis is silent. Only a minority of genetically susceptible individuals develop islet autoantibodies and eventual T1DM. Thus in the natural history of Type 1 diabetes, a subset of autoantibody-positive individuals progress through varying stages of glucose intolerance to clinical diabetes. In Stage 2, there is now serological evidence of humoral (and/or cell-mediated) autoimmunity [i.e., islet cell cytoplasmic autoantibodies (ICA), glutamic acid decarboxylase autoantibodies (GADA), insulinoma-2-associated autoantibodies (IA-2A), or insulin autoantibodies (IAA)] without clinically detectable metabolic perturbations. However during this stage, there can be a 50% decline in beta cell mass without detectable abnormalities by any form of glucose tolerance testing. The earliest functional beta cell abnormality that can be detected (Stage 3) is a decline in first-phase insulin response to intravenously administered glucose. Later, intolerance to oral glucose challenges appears. When there is glucose intolerance Stage 4 is reached. After one to two years of glucose intolerance upon oral testing, a typical history of polyuria, polydipsia, and possible weight loss is identified. Finally, with such frank hyperglycemia, diabetes is clinically diagnosed in Stage 5. Diabetic ketoacidosis may occur if the diagnosis of diabetes is delayed.

Prediction of T1DM:

This can be done by the measurement of islet autoantibodies, HLA class II alleles and β cell function.

Management of T1DM:

The goals of treating a child with DM are to achieve normoglycemia, avoiding metabolic

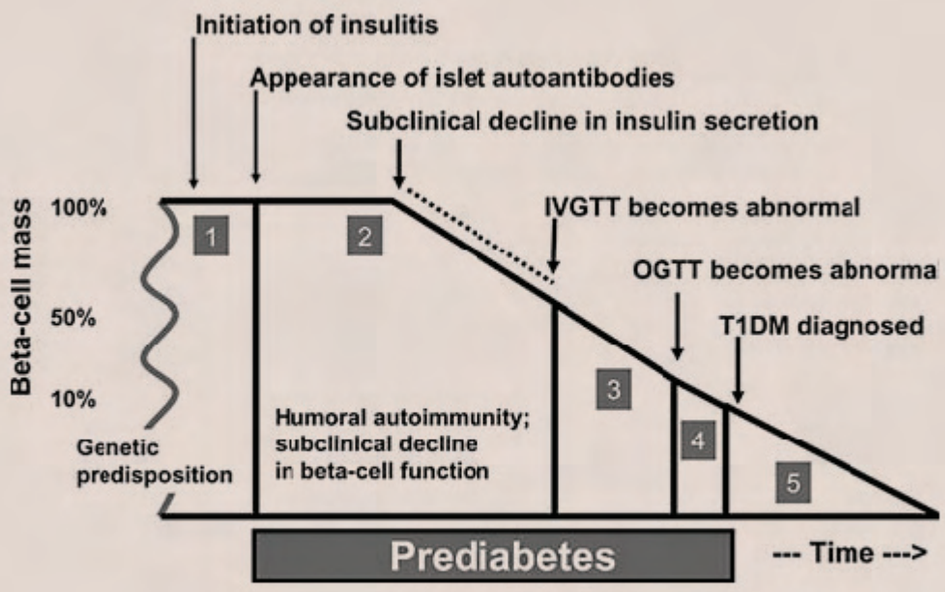


Figure: The natural history of Type 1 diabetes (Abbreviations: IVGTT- intravenous glucose tolerance test; OGTT- oral glucose tolerance test)

decompensation (DKA/Hypoglycemia) along with normal growth and development with prevention of acute and chronic complications of DM. These goals are achieved by coordinated care delivered by a multidisciplinary team, the core of which includes physicians, nursing personnel, diabetes educators, dieticians, social workers and psychologists.

Insulin therapy, diet, exercises and monitoring forms the four cornerstone of diabetes management.

1. Insulin therapy:

The goal of insulin replacement therapy is to mimic the function of β-cell. Current therapy for Diabetes mellitus entails an open loop system with intermittent glucose sensing. Several factors influence the initial daily insulin dose per kilogram of body weight. The dose is usually higher in pubertal children. It is higher in those who have to restore greater deficits of body glycogen, protein, and fat stores and who, therefore, have higher initial caloric capacity. On the other hand, most children with new-onset diabetes have some residual β-cell function (the "honeymoon" period), which reduces exogenous insulin needs. Children with long-standing diabetes and no insulin reserve require about 0.7 U/kg/d if prepubertal, 1.0 U/kg/d at midpuberty, and 1.2 U/kg/d by the end of puberty. A reasonable dose in the newly diagnosed child, then, is about 60–70% of the full replacement dose based on pubertal status. The optimal insulin dose can only be determined empirically, with frequent self-monitored blood glucose levels and insulin adjustment by the diabetes team. Residual β-cell function usually fades within a few months and is reflected as a steady increase in insulin requirements and wider glucose excursions. The initial insulin schedule should be directed toward the optimal degree of glucose control in an attempt to duplicate the activity of the β cell.

All preanalog insulins form hexamers, which must dissociate into monomers subcutaneously before being absorbed into the circulation. Thus, a detectable effect for regular (R) insulin is delayed by 30–60 min after injection. This, in turn, requires delaying the meal 30–60 min after the injection for optimal effect—a delay rarely attained in a busy child's life.

The singular advance in insulin therapy over the

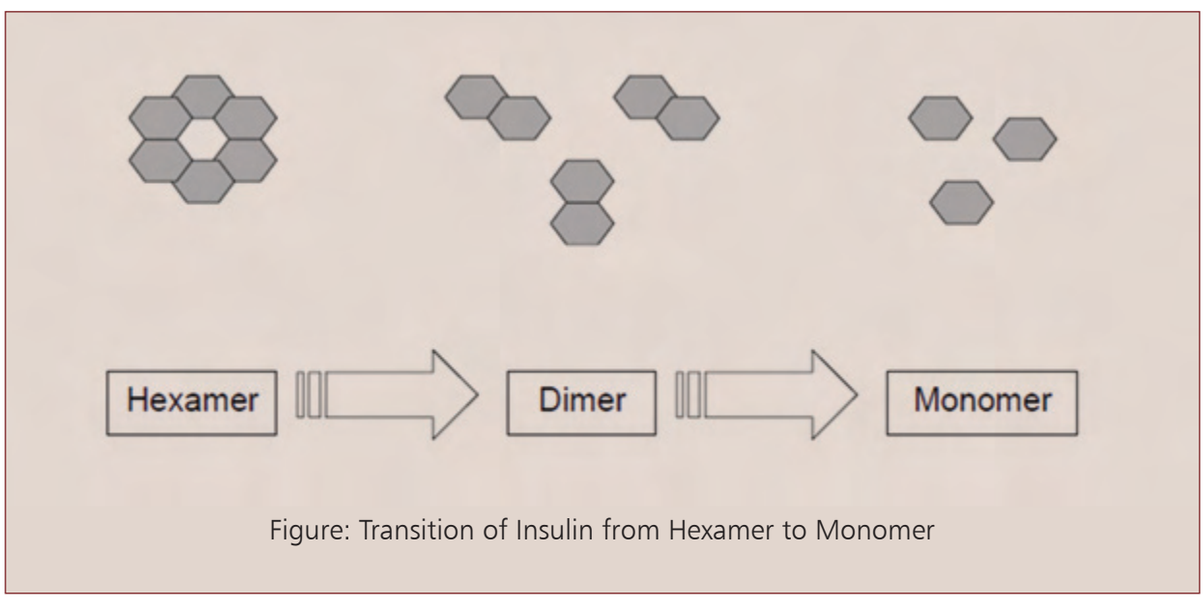


Figure: Transition of Insulin from Hexamer to Monomer

Insulin analogues

Insulin	Structural change	Onset of action	Peak action	Effective duration
Regular		30-60 min	2-3 h	8-10
Rapidly acting analogue:				
Lispro	Lysine- proline conversion in b chain	5-15 min	30-90 min	4-6
Aspart	Aspartic acid for proline in b chain	5-15 min	30-90 min	4-6
Glulisine	Lysine for asparagine substitution in b chain	Rapid		60 min 4
Long acting analogue:				
Glargine	Glycine for asparagines substitution in a chain and a prolonged b chain	2-4 h		No peak 20-24
Detemir dependent	Acylation of lysine in b chain with saturated fatty acid	1 h		90 min Dose

past decade has been the development of insulin analogues. These "designer" insulins, in which the insulin molecule has been modified using recombinant DNA and pharmaceutical chemistry techniques, allow for more predictable time course and dose response than native insulin preparations. The recently introduced inhaled insulin is a different class of insulin analogs that seeks to deliver insulin in more convenient manner than the traditional subcutaneous route of administration. The overall aim of developing insulin analogues is to mimic the physiological release of insulin during the post-prandial and post absorptive periods. The ultra-rapidly acting analogues were developed by altering the amino acid sequence of the insulin molecule to enable rapid dissociation into monomers in subcutaneous tissue and consequent entry into the circulation and rapid (within 5 min of administration) action. These insulins serve to mimic the post-prandial release of insulin from the â cells of the pancreas. The advantages of ultra-rapidly acting insulins is that compared to regular insulin these insulins enable improved control of post-prandial hyperglycemia, and in conjunction with the ultra-long acting analogues in basal-bolus regimens, allow for a more flexible life style with less stringent requirements for timing of meal and snacks.

Newer modes of Insulin therapy:

Continuous subcutaneous insulin infusion (CSII) - CSII has also been used in toddlers and is found to have decreased chances of hypoglycemic seizures.

Inhaled and oral insulin - Pre-prandial inhaled insulin (Exubera) with bedtime long acting injectable insulin achieved same result as conventional insulin regime. Reports of pulmonary fibrosis in a small number of patients necessitate further monitoring and evaluation. Premeal oral insulin (Oralin) has been tried in patients T2DM with promising results.

Typical insulin regimens: There are three main insulin regimens that are used typically in practice.

i) Mixed insulin regimen:

In this regimen, biphasic or mixed insulin is used. This type of insulin contains a mixture of fast-acting (regular) insulin and intermediate-acting (NPH) insulin. The mechanics of this regimen aim to reduce postprandial blood glucose levels and maintain a small amount of circulating background/basal insulin. Difficulties arise with this regimen as there is an overlap of insulin action times at mid-morning and before bedtime. It is during these times that the person is most at risk of having a hypoglycemic episode and may require a small midmorning and bedtime snack to counteract this effect.

ii) Basal bolus insulin regimen:

This course of treatment is based around two very different insulin preparations – a rapid-acting analogue and a long-acting analogue. The long-acting analogue is a once a day subcutaneous injection, which needs to be given at the same time each day. This provides a basal rate of insulin for a 24-hour period. It has a consistent 'flat' profile with no peaks in action, thus making the insulin action reliable and the person less prone to hypoglycemia. This type of insulin should make up 50% of the person's total daily insulin requirements. The remaining 50% of the person's total daily insulin will come from rapid acting analogue insulin. As this has an almost immediate peak action time and is largely broken down after 2–3 hours, this type of insulin is ideal for reducing postprandial blood glucose levels. It can be given immediately before, during, or within 20 minutes of eating a meal. If the insulin is given prior to eating a meal, the person needs to ensure that they do in fact eat all they planned to and had taken insulin for, in order to avoid hypoglycemia. Rapid-acting analogue insulin can also be given as a 'correction dose' between meals if blood glucose levels exceed the normal limits.

iii) Basal insulin regimen:

This type of regimen involves the use of the long-acting analogue insulin and is used for people who have type 2 diabetes who are having difficulties keeping their baseline blood glucose levels within normal range. By having one injection per day of the long-acting analogue insulin can be enough to prevent the overall blood glucose profile from spiraling. This regimen is not suitable for those with type 1 diabetes, as these people require both early (bolus) and late (basal) phase insulin.

Goals of therapy in diabetes

	Conventional therapy	Intensive therapy
Fasting blood glucose	120 - 160mg/dl	80 - 120mg/dl
2 Hour post meal	Not mentioned	<180mg/dl
Bedtime	>100mg/dl	>100mg/dl
HbA1c	7.0 - 8.0%	6.0 - 7.0%

Intensive Insulin Replacement Regimen:

Intensive Insulin replacement strategies stress the importance of administering smaller doses of insulin throughout the day. This approach allows insulin doses to be changed as needed to correct hyperglycemia, supplement for additional anticipated carbohydrate intake, or subtract for exercise. Indeed, bolus-basal treatment with multiple injections is better adapted to the physiologic profiles of insulin and glucose and can therefore provide better glycemic control than the conventional 2- to 3-dose regimen. Age-adjusted and individualized insulin to carbohydrate ratios and insulin dosage adjustment algorithms have been developed to normalize elevated blood glucose levels and to compensate for alterations in carbohydrate intake. The use of flexible multiple daily injections (FMDIs) and CSII in children with T1DM improves glycemic control without an increase in the incidence of severe hypoglycemia.

Insulin therapy in special situations:

Management during Surgery:

Surgery can disrupt glucose control in the same way as can intercurrent infections. Stress hormones associated with the underlying condition as well as with surgery itself decrease insulin sensitivity. This increases glucose levels, exacerbates fluid losses, and may initiate DKA. On the other hand, caloric intake is usually restricted, which decreases glucose levels. The net effect is as difficult to predict as during an infection. Vigilant monitoring and frequent insulin adjustments are required to maintain euglycemia and avoid ketosis. Maintaining glucose control and avoiding DKA are best accomplished with IV insulin and fluids. The IV insulin is continued after surgery as the child begins to take oral fluids; the IV fluids can be steadily decreased as oral intake increases. When full oral intake is achieved, the IV may be capped and subcutaneous insulin begun. When surgery is elective, it is best performed early in the day, allowing the patient maximal recovery time to restart oral intake and subcutaneous insulin therapy. When elective surgery is brief (less than 1 hr) and full oral intake is expected shortly afterward, one may simply monitor the blood glucose hourly and give a dose of insulin analog according to the child's home glucose correction scale. If glargine or detemir is used as the basal insulin, a full dose is given the evening before planned surgery. If NPH or Lente is used, one half of the morning dose is given before surgery. The child should not be discharged until blood glucose levels are stable and oral intake is tolerated.

Guidelines for Intravenous Insulin coverage during surgery

Blood Glucose Level (mg/dl)	Insulin Infusion (U/Kg/hr)	Blood Glucose Monitoring
<120	0.00	1 hr
121–200	0.03	2 hr
200–300	0.06	2 hr
300–400	0.08	1 hr
400	0.10	1 hr

An infusion of 5% glucose and 0.45% saline solution with 20 mEq/L of potassium acetate is given at 1.5 times maintenance rate.

Management during Infections : The overall goals are to maintain hydration, control glucose levels and avoid ketoacidosis. This can usually be done at home if proper sick day guidelines are followed and through telephone contact with health care providers. The family should seek advice if home treatment does not control ketonuria, hyperglycemia, or hypoglycemia, or if the child shows signs of dehydration.

Adjunctive therapies to insulin: In some of the subjects adjunctive therapy may help in improving glycemic control. Adjunctive therapies can be grouped into the following categories based on the mechanism of action:

(i) Insulin sensitizing agents such as biguanides and thiazolidinediones.

The biguanide (metformin), has been used in T1DM individuals in whom insulin resistance (generally secondary to obesity) is a marked feature.

(ii) Medications altering gastrointestinal nutrient delivery (acarbose and amylin) –

These agents serve to decrease post-prandial hyperglycemia.

(iii)Other targets of action - Pirenzepine, insulin-like growth factor-1 (IGF-1), or glucagons like peptide-1.

Many of these agents have been found to be effective in short-term studies with decrease in glycosylated hemoglobin of 0.5-1.0 per cent, lower levels of postprandial blood glucose, and decreased daily insulin requirements. Adverse effects such as poor gastrointestinal tolerability (metformin, acarbose) or potential acceleration of retinopathy (IGF-1) re-emphasize the need for further studies of efficacy, safety, and patient selection before these adjunctive therapies can be routinely recommended for patients with T1DM.

Sick days rules

1) Daily insulin dose should never be omitted irrespective of food intake

2) Blood glucose and urine ketones to be monitored every 4 hrly. Extra insulin (10-20%) to be given if blood glucose is >250mg/dl.

3) If blood glucose is <100mg/dl, sweet liquids /IV fluids may be given but insulin should not be stopped.

4) Hospitalization is essential if, there is excessive vomiting, breathlessness, drowsiness or ketones are rising despite extra insulin.

Pancreatic and Islet cell transplantation:

At present lifelong administration of exogenous insulin is the mainstay of treatment regimens for T1DM. However, innovative treatment protocols aimed at replacing β cell via pancreatic organ transplantation or islet cell transplantation provide a hope for a cure.

Pancreatic transplantation is indicated in individuals with end-stage renal disease or those with severe metabolic complications in whom the benefits outweigh the risks of surgical procedure and prolonged immunosuppression. However, in children and adolescent who do not have such dire complications, pancreatic organ transplantation is not a practical option.

Islet cell transplantation, in which islets cells isolated from pancreas of cadavers are perfused percutanoeusly into the portal vein, has the advantage of being a minimally invasive procedure compared to pancreas transplantation.

Edmonton protocol - The salient features of this protocol are the use of adequate islet mass for transplantation by repeated administration of high quality islet cells, and a novel corticosteroid-free anti rejection combination of interleukin-2 receptor monoclonal antibody, sirolimus, and low dose tacrolimus. Availability of islet cells which is currently only available from cadaveric pancreas is a limiting factor.

2. Diet:

The recommended diet for a child with diabetes is nothing but a healthy, balanced, normal diet with the additional requirement of avoidance of simple sugars. The meal plan should be based on the family eating habits with minimum necessary changes. Food should be divided in three main meals (breakfast, lunch, dinner) and 2-3 mid meal snacks. Total calories should be enough to maintain ideal body weight and promote growth.

Glycemic index is a measure of the rate of rise of blood sugar after a particular type of food is eaten, in comparison with glucose, which is taken as 100. This index depends not only on the type of carbohydrate and its fiber content, but also upon the way it is cooked.

Within a major food group, low glycemic index foods may be preferred over high GI foods. Examples of Indian foods with low GI are pulses with skin, like red kidney beans (rajma), chappati made of wheat and gram flour, oat porride, green vegetables and fruits (apple, guava, peach, orange).

Nutrient recommendations and distribution

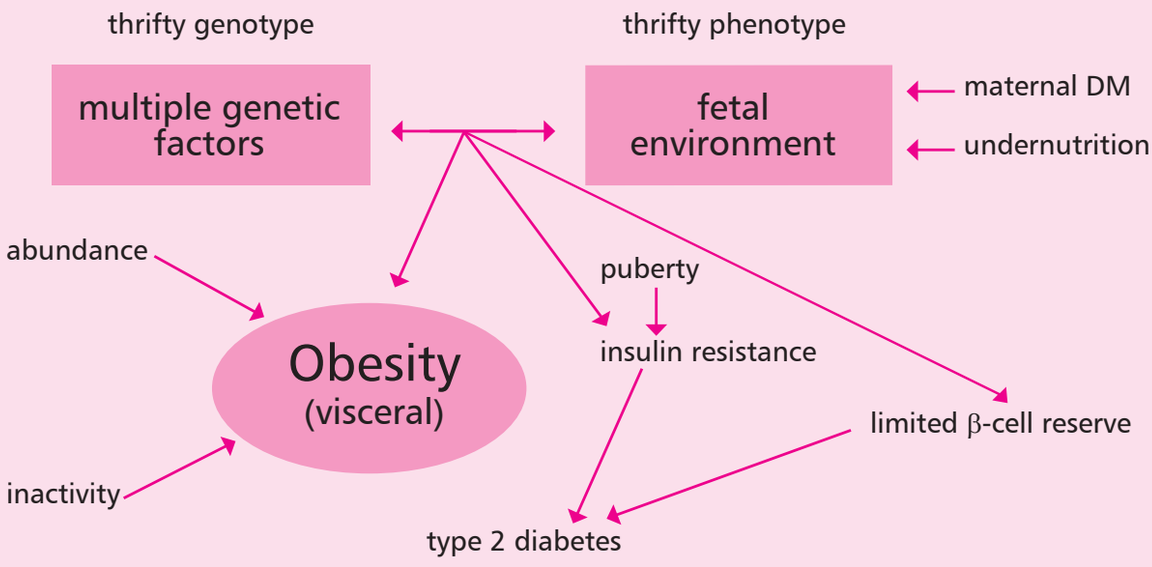
Nutrient	(%) of Calories	Recommended Daily Intake
Carbohydrate	Will vary	High fiber, especially soluble fiber; optimal amount unknown
Fiber	>20 g per day	
Protein	12–20	
Fat	<30	
Saturated	<10	
Polyunsaturated Monounsaturated	6–8 Remainder of fat allowance	
Cholesterol Sodium		300 mg Avoid excessive; limit to 3,000 – 4,000 mg if hypertensive

3. Exercise:

Physical activity of all kinds should be encouraged, for example, running, swimming, foot-ball, hockey, skipping, or an exercise bicycle. Benefits of sports include better self esteem and sense of well being with improved cardiovascular benefits and decreased lipids in the serum. Although exercise improves insulin sensitivity, there is no evidence that it controls overall metabolic control. Insulin regimes can be modified according to exercise demand. Insulin can be decreased by 10-20% with strenuous exercise. Provision should be made for extra calories before exercise, to prevent hypoglycemia.

4. Monitoring of blood glucose:

Self-monitoring of blood glucose (SMBG) is an essential component of managing diabetes. Monitoring often also needs to include insulin dose, unusual physical activity, dietary changes, hypoglycemia, intercurrent illness, and other items that may influence the blood glucose. These items may be valuable in interpreting the SMBG record, prescribing appropriate adjustments in insulin doses, and teaching the family. Parents and patients should be taught to use these devices and measure blood glucose at least 4 times daily - before breakfast, lunch, and supper and at bedtime. When insulin therapy is initiated and when adjustments are made that



Factors implicated in the development of T2DM

may affect the overnight glucose levels, SMBG should also be performed at 12 a.m. and 3 a.m. to detect nocturnal hypoglycemia. Ideally, the blood glucose concentration should range from approximately 80 mg/dL in the fasting state to 140 mg/dL after meals. In practice, however, a range of 60–220 mg/dL is acceptable, based on the age of the patient. Blood glucose measurements that are consistently at or outside these limits, in the absence of an identifiable cause such as exercise or dietary indiscretion, are an indication for a change in the insulin dose. If the fasting blood glucose is high, the evening dose of long-acting insulin is increased by 10–15% and/or additional fast-acting insulin (lispro or aspart) coverage for bedtime snack may be considered. If the noon glucose level exceeds set limits, the morning fast-acting insulin (lispro or aspart) is increased by 10–15%. If the pre-supper glucose is high, the noon dose of fast-acting insulin is increased by 10–15%. If the pre-bedtime glucose is high, the pre-supper dose of fast-acting insulin is increased by 10–15%. Similarly, reductions in the insulin type and dose should be made if the corresponding blood glucose measurements are consistently below desirable limits.

Type 2 diabetes in Childhood:

About 8% of children and adolescents from a tertiary clinic in India with onset of diabetes before 18 years of age had T2DM. It has been shown that, on average, for every 1 kg increase in body weight a person has a 9% relative increase in the risk of developing type 2 diabetes

Etiology:

The thrifty phenotype hypothesis states that poor nutrition in fetal and early infant life would be detrimental to the development and function of the beta cells and insulin-sensitive tissues, primarily muscle, leading to insulin resistance. With obesity in later life, T2DM would develop. This hypothesis explains the effect of fetal nutrition on later glucose tolerance and other manifestations of insulin

insensitivity, such as hypertension and increased cardiovascular problems. These findings could also be interpreted as a reflection of the thrifty genotype hypothesis that defective insulin action in utero results in decreased fetal growth and obesity-induced impaired glucose tolerance in later childhood or adulthood

The Role of Race, Gender, and Family History:

There is a racial difference in the insulin responses to various stimuli that parallels the ethnic/racial differential in T2DM frequency. Greater insulin responses to oral glucose are seen in African-American children and adolescents than in European-American children after adjustments are made for weight, age, ponderal (obesity) index, and pubertal stage. Girls are more insulin resistant than boys as early as five years of age. Girls carry 26% more subcutaneous fat than boys, which may contribute to the development of insulin resistance in the female population.

Genetic Considerations:

The evidence that T2DM is a genetic disease includes: the family clustering and segregation analyses that indicate that siblings of affected individuals have 3.5 times the general population risk of developing T2DM; studies of monozygotic twins that indicate a concordance of 80% to 100%, greater than twice the concordance for T1DM in dizygotic twins and in monozygotic twins.

The Role of Obe sity:

The insulin resistance associated with obesity is the fundamental problem in T2DM in children and adolescents, as it is in adults. Total obesity is not as important as location of adipose tissue in causing insulin resistance. Visceral fat is more metabolically active than subcutaneous fat and produces adipokines that cause insulin resistance, thus predisposing to T2DM. The amount of visceral fat in obese adolescents correlates directly with basal and glucose-stimulated insulin levels and inversely with insulin sensitivity. With increasing BMI, insulin stimulated glucose metabolism decreases while fasting insulinemia increases.

The Role of Fetal and Childhood Nutrition:

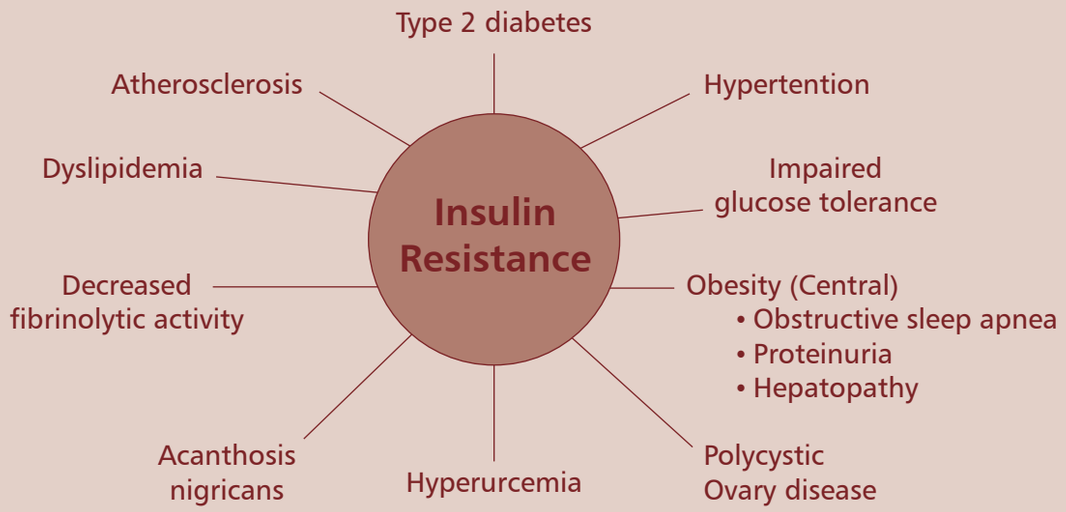
The association of lower birth weight, smaller head circumference, and thinness at birth with later development of insulin resistance and impaired glucose tolerance or T2DM suggested in utero programming that limited beta-cell capacity and induced insulin resistance in peripheral tissues.

Early childhood nutrition also plays a role in the development of insulin resistance later in life. An association between high protein intake in infancy and later obesity has been suggested. Breast feeding results in a more appropriate caloric intake at a critical stage in development than bottle feeding which is more likely to be associated with overfeeding and obesity.

The Role of Puberty:

Puberty is associated with relative insulin resistance, reflected in a two- to threefold increase in the peak insulin response to oral or intravenous glucose; insulin-mediated glucose disposal is approximately 30% lower in adolescents than in prepubertal children or young adults. The physiologic insulin resistance of puberty is of no consequence in the presence of adequate beta-cell function. The cause of this physiologic resistance is likely the transitory increased activity of the growth hormone–insulin growth factor axis, which coincides with the physiologic insulin resistance of adolescence.

Prevention of T2DM: Primary prevention would involve intervention to prevent the development of obesity or to correct obesity before the development of other features of insulin resistance syndrome



Co morbidities of insulin resistance

Screening for type 2 DM:

The American Diabetes Association recommends that all children over 10 years, who are overweight (>85th centile for age or weight>120% of the 50th centile for height by national standards) and having any two of the following risk factor, should be screened for DM, every two years with fasting plasma glucose.

Family history of T2DM in first or second degree relative,

Polycystic ovaries,

Acanthosis nigricans,

Dyslipidemia,

Hypertension,

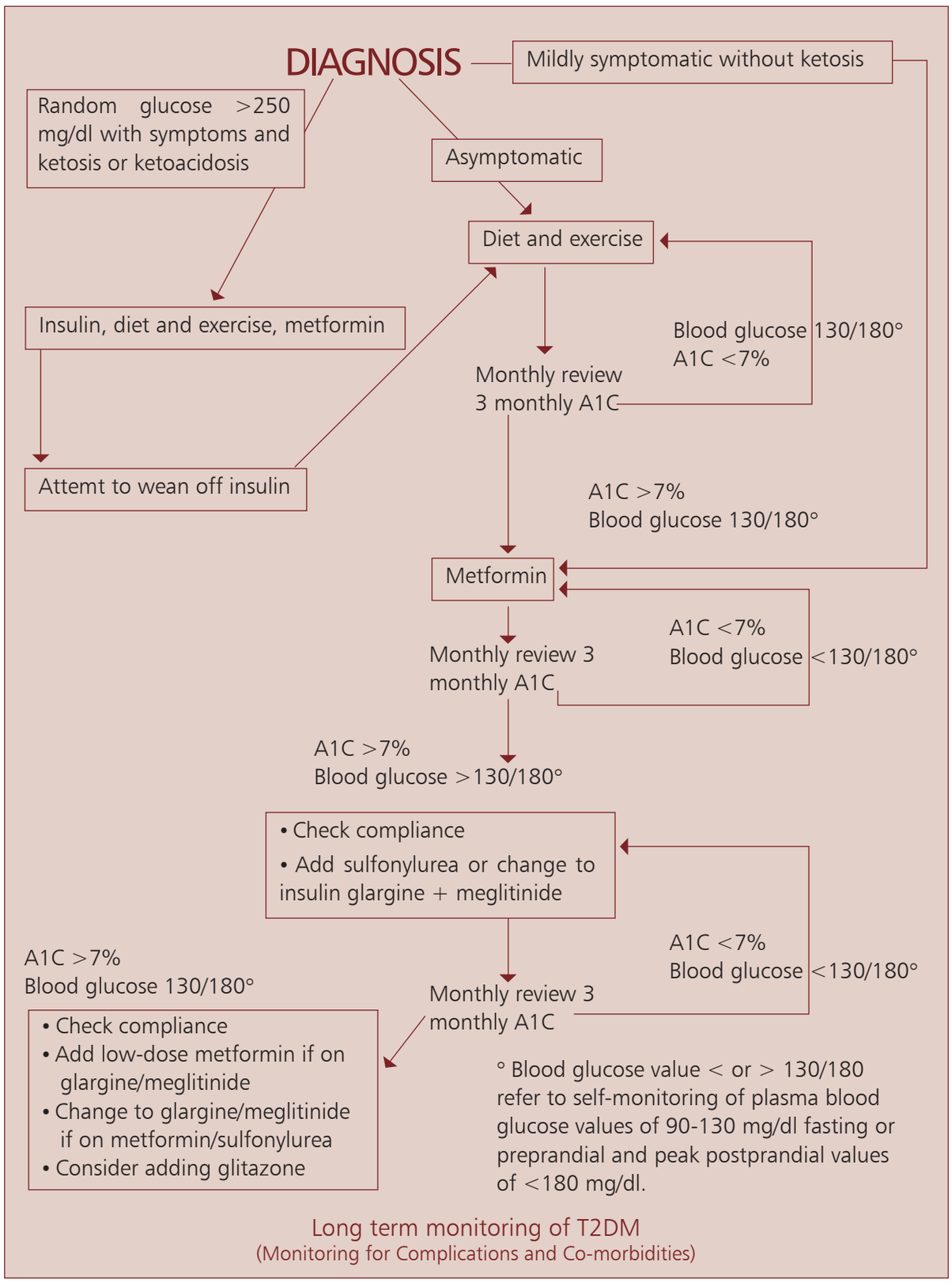
Ethnic group.

Presence of Turner, Klinefelter, Prader-willi or Cushings syndromes warrants screening irrespective of presence of obesity.

Diabetes Mellitus of the newborn:

Transient- Neonatal diabetes mellitus is rare, with an estimated incidence of 1 per 100,000 newborns. It occurs most often in infants who are small for gestational age and is characterized by hyperglycemia and pronounced glycosuria, resulting in severe dehydration and, at times, metabolic acidosis but with only minimal or no ketonemia or ketonuria. Insulin responses to glucose or tolbutamide are low to absent; basal plasma insulin concentrations are normal. After spontaneous recovery, the insulin responses to these same stimuli are brisk and normal, implying a functional delay in β-cell maturation with spontaneous resolution. Abnormalities of chromosome 6 are common in transient neonatal DM. Administration of insulin is mandatory during the active phase of DM in the newborn. One to two U/kg/24 hr of an intermediate-acting insulin in two divided doses usually results in dramatic improvement and accelerated growth and gain in weight.

Permanent- DM in the newborn period may be permanent if associated with the rare syndrome of pancreatic agenesis. Activating



Long term monitoring of T2DM
(Monitoring for Complications and Co-morbidities)

CONDITION	SCREENING TEST	COMMENT
Hypertension	Blood pressure	
Fatty liver	AST, ALT, possibly liver ultrasound	
Polycystic ovary	Menstrual history, assessment for androgen excess with	
syndrome	free/total testosterone, DHEA	
Microalbuminuria	Urine albumin concentration and albumin/creatinine ratios	
Dyslipidemia	Fasting lipid profile (total, LDL, HDL cholesterol, triglycerides)	Obtain at diagnosis and every 2 years
Sleep apnea	Sleep study to assess overnight oxygen saturation	

mutations in the ABCC8 gene encoding the ATP-sensitive potassium-channel subunit Kir6.2 producing permanent neonatal diabetes has been described in infants. Dominant mutations in ABCC8 account for about 12% of cases of neonatal diabetes. Sulfonylurea therapy is more effective than insulin in diabetes due to ABCC8 mutations.

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Gestational Diabetes Mellitus (GDM)

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Introduction:

Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance of varied severity with onset or first recognition during the present pregnancy.

GDM affects 3-10% of pregnancies.

The women with GDM are usually asymptomatic and the diagnosis of the condition is by screening during pregnancy. These women are at increased risk for developing pre-eclampsia, operative deliveries and type II diabetes after pregnancy.

Babies born to these GDM mothers are at increased risk of being large for gestational age, hypoglycaemia and jaundice. They are prone to develop childhood obesity with type II diabetes later in life.

Gestational diabetes is a treatable condition and adequate sugar control can effectively decrease the associated risks. Most patients are treated only with diet modification and moderate exercise but some may require anti- diabetic drugs, including insulin.

Carbohydrate metabolism during regnancy:

Pregnancy is a diabetogenic condition. The most important reasons that pregnancy uncovers the diabetic tendencies of asymptomatic women, are due to:

- Insulin resistance.
- Increased anti-insulin effects of cortisol, estriol and progesterone during pregnancy.
- Production of placental somatomammotropins
- Insulin destruction by the kidney and placental insulinase.
- Increased Lipolysis.
- The mother uses fat for her caloric needs and saves glucose for the foetal needs.
- Changes in Gluconeogenesis.
- The foetus uses preferentially alanin and other amino acids and deprives the mother of a major gluconeogenic source.

Effects of gestational diabetes on the mother:

- Pre-Eclampsia: Pre-Eclampsia is associated with 10 – 25% of GDM pregnancies.
- Operative delivery: Foetal macrosomia necessitates the need for Caesarean section in these mothers.
- Post partum haemorrhage: Exaggerated uterine distention either due to foetal macrosomia or polyhydroamnios can lead to increased incidence of atonic post partum bleeding.

Effects of gestational diabetes on the foetus:

- Foetal anomalies: Unlike in women with overt diabetes, incidence of foetal anomalies is not increased with GDM.
- Macrosomia: It is defined by the American College of Obstetricians and Gynaecologists, as infant whose birth weight exceeds 4500g.Incidence is 17-29%. Macrosomia is due to maternal hyperglycaemia, which causes foetal hyperinsulinaemia. This foetal hyperinsulinaemia in turn stimulates excessive somatic growth.
- Traumatic delivery: Infants of mother with GDM have excessive fat deposition on the shoulders and trunk, which predisposes to shoulder dystocia. Brachial plexus injury and clavicular fractures are also likely at the time of delivery.
- Unexplained stillbirth: Gestational diabetes with elevated fasting glucose has been associated with unexplained stillbirth.
- Neonatal hypoglycaemia: Neonatal hyperinsulinemia may provoke hypoglycaemia within minutes of birth. According to American Diabetic Association, neonatal glucose values less than 35mg/dl at term are considered abnormal.
- Neonatal complications: These neonates are prone for jaundice, polycythemia, hypocalcemia and hypomagnesemia.
- Respiratory distress syndrome (RDS): GDM interferes with foetal lung maturation and impairs surfactant synthesis causing dysmature babies prone to RDS.

Effects of pregnancy on diabetes:

- More insulin is necessary to achieve metabolic control.
- Progression of diabetic retinopathy
- Worsening of diabetic nephropathy
- Increased risk of death for patients with diabetic cardiomyopathy.

Detection of Gestational Diabetes:

Screening:

Chicago workshop conference on GDM (1990), recommended universal screening, as about 40-60% of women with GDM have no demonstrable risk factor. Women at high risk for GDM should be screened for diabetes as soon as possible after the confirmation of pregnancy.

Criteria for high-risk are:

- Obesity (> 15% of non-pregnant ideal body weight)
- Diagnosis of Polycystic Ovarian Disease
- Positive family history of diabetes (sibling or parent)
- Poor reproductive history (more than 3 spontaneous abortions)
- History of congenital anomaly
- History of still birth, unexplained neonatal death
- History of premature delivery
- History of delivery of a large infant (>4000gm)
- History of traumatic delivery with associated neurological disorder in the infant
- History of diabetes in previous pregnancy

- History of pre-eclampsia as a multipara
- Presence of glycosuria
- Polyhydramnios
- Recurrent severe moniliasis
- Recurrent urinary tract infection
- Chronic hypertension

All women who are at low risk of GDM, including those above, who have not found to have diabetes early in pregnancy, should undergo the screening glucose challenge test (sometimes called the O'Sullivan test) between 24–28 weeks. Measurement of plasma glucose one hour after ingesting 50 gm of glucose without regard to time of day or last meal if exceeds 140mg /dl (7.8 mmol/l), is used as the cut-off for performing the diagnostic 100gm 3 hours glucose tolerance test.

Diagnostic criteria:

100gm 3 hours glucose tolerance test should be performed in the morning after an overnight fast of at least 8 hours.

American College of Obstetricians and Gynaecologists and National Diabetes Data Group suggest reference plasma glucose values recommended by Carpenter and Coustan:

Fasting $\geq$ 95 mg/dl

1-hour $\geq$ 180 mg/dl

2-hour $\geq$ 155 mg/dl

3-hour $\geq$ 140 mg/dl

The diagnosis of GDM is made when minimum two values are met or exceeded.

Management of GDM:

Diet:

Nutritional Counseling is the corner stone in management of GDM. The objective is to provide the calories and nutrients necessary for the mother and the foetus without causing postprandial hyperglycaemia. Good glycaemic control significantly improves incidence of macrosomia and results in fewer caesarean deliveries.

The American Diabetic Association (2000) recommends nutritional counseling with individualization based on height, weight and a diet that provides an average of 30 kcal/kg/day of pre-pregnant body weight for non-obese women and 25kcal/kg/day for overweight women.

For majority of women with GDM, the optimal total daily caloric intake is between 2000 and 2500 kcal/day. In third trimester an additional 300kcal are required. The total caloric intake is split into two to three meals and snacks. This caloric allowance is distributed in 40-50% complex carbohydrates, 30-40% fat (unsaturated) and proteins. The majority of the dietary carbohydrate should be in the form of unrefined, high-fiber foods.

Maternal ketonemia has been linked with impaired psychomotor development in the child. Therefore, it is customary to check the urine for ketones in women ingesting restricted number of calories and if the urine starts to show consistently marked acetonuria (>3+), the amount of dietary carbohydrate needs to be increased.

Exercise:

Upper body exercises placing little mechanical stress on the trunk, improve cardio-respiratory fitness. Regular exercise along with diet therapy helps to reduce blood glucose levels and hence the need for the drug therapy.

Hypoglycemic Agents:

- Insulin: Insulin therapy is initiated in women with gestational diabetes if fasting glucose levels at less than 105 mg/dl or 2 hours post

lunch plasma glucose less than 120 mg/dl are not consistently maintained despite diet therapy and exercise for 2 weeks. Generally, a total dose of 20-30 Units of short acting insulin is required in divided doses daily. Insulin therapy is initiated by introducing the dose before breakfast. Adding short acting insulin before meals can control postprandial hyperglycaemia.

- Metformin: Treatment of polycystic ovarian syndrome with metformin during pregnancy has been noted to decrease the incidence of GDM. Incidence of preterm delivery is less in Metformin-treated women whereas; severe neonatal hypoglycemia is less common in insulin-treated women.

- Glyburide(Glibenclamide): It is nonteratogenic sulfonylurea group hypoglycaemic agent belonging to category B drug .It stimulates release of insulin from the storage granules of the pancreatic beta cells and decreases insulin resistance. It can be given as 2.5 mg once or twice daily maximum up to 20 mg.

Blood Glucose Monitoring:

The objective of treatment is to maintain the fasting capillary glucose at less than 95 mg/dl or the 1-hour or 2-hour postprandial less than 140 mg/dl and 120mg/dl, respectively.

Patient should be taught self-monitoring of her capillary glucose levels using her own machine. She should be instructed to report to the physician for further instructions if the blood glucose values noted are above or below expected. Regular blood samples including glycosylated Hb (Hb A1C) levels gives an idea of glucose control over a longer time period.

Obstetric Management:

Fetal surveillance: Low risk gestational diabetic patients who achieve adequate control with diet alone and do not develop macrosomia, polyhydramnios, or pre-eclampsia do not require fetal surveillance testing before 40wks. High risk gestational diabetics and patients on insulin should have antepartum fetal surveillance testing with daily foetal movement count, weekly or biweekly NST or Modified Biophysical Profile starting at 34 weeks of gestation.

Planning delivery:

Elective induction prior to term is not indicated in low-risk gestational diabetics. They can be allowed to develop spontaneous labour. If pregnancy prolongs more than 40 weeks then foetal birth weight should be estimated with the help of ultrasonography. Labour induction is considered if estimated foetal weight is less than 4 kg. In case of failed induction of labour or estimated weight more than 4 kg pregnancy should be terminated by lower segment caesarean section.

High-Risk gestational diabetics who are likely to develop foetal macrosomia are electively induced at 38 completed weeks to curtail foetal growth and prevent shoulder dystocia. In case of failed induction of labour or estimated weight more than 4 kg pregnancy should be terminated by lower segment caesarean section.

Intrapartum care:

Most insulin treated GDM do not need insulin during labour or after vaginal or caesarean delivery. Usually, Capillary Blood Glucose is measured every 2-4 hrs during labour and upward deviations from normal are corrected with small doses of regular insulin or low dose intravenous insulin to maintain blood glucose between 100 and 120 mg/dl. Careful intrapartum foetal heart monitoring is done to detect foetal distress at the earliest.

Postpartum recommendations:

Women diagnosed with gestational diabetes have an increased risk of developing type II diabetes mellitus in the future. The risk is highest in women who needed insulin treatment, had antibodies associated with diabetes (such as antibodies against glutamate decarboxylase, islet cell antibodies and/or insulinoma antigen-2), women with more than two previous pregnancies, and women who are obese.

The Fourth International Conference on GDM recommended that women diagnosed with gestational diabetes undergo evaluation with 75g oral GTT at 6 to 12 weeks after delivery.

Women with normal oral GTT should be reassessed at a minimum of 3-year interval (American Diabetic Association, 2003).

Women who required treatment with insulin or glyburide, had elevated fasting serum glucose levels during pregnancy or those diagnosed with gestational diabetes at 24 wks, should undergo 75g OGTT. There is 50 % likelihood of women with gestational diabetes developing overt diabetes within 20years.

If fasting hyperglycaemia develops during pregnancy, diabetes is more likely to persist postpartum.

Requirement of insulin therapy during pregnancy and especially before 24weeks is a powerful predictor of diabetes after the pregnancy.

Women with gestational diabetes are also at risk for cardiovascular complications associated with abnormal serum lipids, hypertension and abdominal obesity-the Metabolic Syndrome.

Obese women were more likely to have impaired glucose intolerance in subsequent pregnancies.

Our Experience with Gestational Diabetes :

At BARC hospital, universal glucose screening using 50gm oral glucose irrespective of the time of the day or the last meal, is recommended for all pregnant women between 24 and 28 weeks. Women with high risk factors like advanced maternal age, obesity, hypertension, family history of diabetes, gestational diabetes in previous pregnancy and a prior macrosomic, malformed or still born foetus are found to be benefited from early screening. Even if screening in early pregnancy for these women yields normal results, subsequent screening is redone at 24 to 28 weeks, as per ACOG guidelines.

Plasma glucose value at 1 hour exceeding 140 mg/dl is used as the cut off for performing the diagnostic 100 gm -3 hours oral glucose tolerance test. Two or more values above the normal with reference to Carpenter and Coustan criteria are diagnostic of gestational diabetes. These women are advised appropriate diet control and exercise. Fasting and post lunch plasma glucose is repeated after two weeks of strict dietary control and exercise.

Insulin therapy is instituted when standard dietary management along with exercise does not consistently maintain the fasting plasma glucose at less than 105 mg/dl or post lunch plasma glucose less than 120 mg/dl. Hospitalization is advised to initiate insulin therapy to safely titrate the dose according to capillary glucose monitoring and to educate the patient for self-administration and self-monitoring of insulin. Patient is discharged on insulin once adequate sugar control is achieved. Regular blood glucose monitoring is performed with antenatal check up and antenatal foetal surveillance by daily foetal kick count, ultrasound, and non-stress test. GDM interferes with lung maturation and impairs surfactant synthesis causing dysmature babies prone to RDS. Hence, foetal lung maturity is delayed even at 36 weeks in infants born to mothers with GDM.

If patient needs delivery prior to term, two doses of injection betamethasone (12 mg) intramuscularly are advocated at 24 hours interval to achieve foetal lung maturity. Additional increment of insulin dose is needed to compensate this steroid induced hyperglycaemia. High-Risk gestational diabetics who are likely to develop foetal macrosomia are electively induced at 38 completed weeks to curtail foetal growth and prevent shoulder dystocia. If pregnancy prolongs more than 40 weeks in low risk GDM then foetal birth weight on ultrasonography is estimated along with amniotic fluid volume. Labour induction is considered if estimated foetal weight less than 4 kg. In case of failed induction of labour or estimated weight more than 4 kg lower segment caesarean section is performed. Post pregnancy blood glucose monitoring is advised for early detection of type II diabetes in these high-risk women.

Summary:

Universal screening and diagnosis of GDM, not only helps to improve the pregnancy outcome but also acts as a first warning sign for these women, who are at risk of developing type II diabetes in later life. Timely lifestyle behavioral changes, including weight control and exercises are valuable strategies to prevent type II diabetes and its long-term complications.

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Diabetic Foot

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Introduction

India has more than 30 million people with diabetes. The numbers of diabetics climb steeply day by day. It is estimated that by 2025, India will be number one in the world with the maximum number of people with diabetes. Ten to fifteen percent of diabetic patients develop foot ulcers at some point in their lives and foot related problems are responsible for up to 50% of diabetes related hospital admissions. Once patients develop an ulcer, they carry a 10% to 30% chance of progressing to an amputation.

Patho-physiology In Diabetic Foot:

1. Sensory and autonomic neuropathy:

Distal symmetric polyneuropathy is perhaps the most common complication affecting the lower extremities of patients with diabetes mellitus. This complication occurs in up to 58 percent of patients with longstanding disease.

The major peripheral neuropathy in diabetes is a sensory symmetric polyneuropathy, with a denervation of the longest nerves of the feet with progression upward in a stocking distribution. Sensory neuropathy presents in the classic "glove and stocking" distribution, symmetrically affecting the toes first and gradually moving proximally. Losses in deep tendon reflexes, proprioception, vibratory, pain and light touch sensation are the most common findings, collectively called "negative" symptoms. Conversely, painful neuropathy is a distressing manifestation of peripheral neuropathy consisting primarily of "positive" symptoms, such as burning, gnawing, or lancinating pains that worsen at night. Although the discomfort may begin as a sensory phenomenon that manifests as increased sensitivity (hyperalgesia) and pain, the progression of the disease often leads to complete insensitivity of one or both feet.

This lack of protective sensation, combined with unaccommodated foot deformities, exposes patients to undue sudden or repetitive stress. The individual who has neuropathy may suffer penetrating injury of the soft tissues caused by a foreign body and being unable to sense the pain or the foreign body, will continue to ambulate and deepen the wound. The clinical correlates are to avoid walking barefoot or in socks alone, to avoid unprotected exposure of the toes with sandals and to monitor for foreign bodies in shoes.

Autonomic dysfunction can lead to dry skin with cracks or fissures that may serve as entry portals for bacterial infections in the compromised foot. These are common precursors to ulceration and infection in the diabetic population.

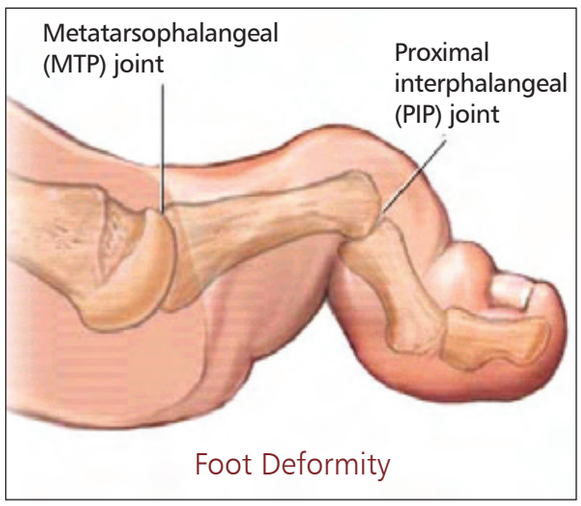
Motor neuropathy results in muscle weakness, atrophy, dysfunction and gait disturbance. Clinical manifestations include footdrop from anterior crural muscle atrophy or characteristic hammer toes from intrinsic muscle atrophy (intrinsic minus foot). These changes transfer stress to the forefoot, leading to increased pressure in these areas and thus they increase the potential for breakdown and ulceration both on the plantar metatarsal heads and dorsal proximal interphalangeal joints (hammertoe).

2. Peripheral arterial occlusive disease:

Peripheral arterial occlusive disease is four times more prevalent in diabetics than in nondiabetics. Smoking, hypertension and hyperlipidemia commonly contribute to the increased prevalence of peripheral arterial occlusive disease in diabetics.

Overall, people with diabetes have a higher incidence of atherosclerosis, thickening of capillary basement membranes, arteriolar hyalinosis and endothelial proliferation. Calcification and thickening of the arterial media (Mönckeberg sclerosis) are also noted with higher frequency in the diabetic population

The presence of lower extremity ischemia is suggested by a combination of clinical signs and symptoms plus abnormal results on noninvasive vascular tests. Patients may have additive effects on the peripheral circulation caused by underlying hypertension, hypercholesterolemia and cigarettes. People who have PAD may have symptoms of intermittent claudication with the level pain situated at the level of the arterial insufficiency. More severe ischemia maybe associated with nocturnal pain and progression to rest pain. Other signs are absent popliteal or posterior tibial pulses, thinned or shiny skin, absence of hair on the lower leg and foot, thickened nails, redness of the affected area when the legs are dependent, or "dangled," and pallor when the foot is elevated.



Foot Deformity

Proper control of concomitant hypertension or hyperlipidemia can help to reduce the risk of peripheral arterial occlusive disease. Smoking cessation is essential for preventing the progression of occlusive disease.

3. Structural Deformity and Limited Joint Mobility:

Most diabetic foot ulcers form over areas of bony prominences, especially when bunions, calluses or hammer-toe formations lead to abnormally prominent bony points. Foot deformities are believed to be more common in diabetic patients due to atrophy of the intrinsic musculature responsible for stabilizing the toes. People who have peripheral neuropathy may have loss of normal motor tone with resultant limited joint mobility and abnormal rigidity to joint flexion.

4. Susceptibility to infection:

Susceptibility to infection and impairment in the ability to fight established infections has long been recognized as significant factors in the etiology of diabetic foot infections, ulceration and gangrene. Although infection is infrequently a direct cause of ulceration, ulcers can be infected and often place the limb at risk of amputation. The diabetic patients' "immunopathy" is caused by a deficiency in the phagocytic activity of leukocytes, impaired intracellular bacterial killing and a defect in normal chemotactic mechanisms. Even common pathogens can result in overwhelming infections, especially in the presence of neuropathy and ischemia. Usually "benign" bacteria such as Staphylococcus epidermidis or enterococci assume extremely pathogenic roles in the diabetic milieu.

Prevention of diabetic foot infection:

Patient education regarding foot hygiene, nail care and proper footwear is crucial to reducing the risk of an injury that can lead to ulcer formation. The vast majority of diabetic foot complications resulting in amputation begin with the formation of skin ulcers. Early detection and appropriate treatment of these ulcers may prevent up to 85 percent of amputations. Research has shown that diabetic people, who take good care of their feet and protect their feet from injury, are much less likely to develop foot ulcers. The patient and family members have the responsibility for performing the daily tasks that focus on prevention of problems.

The most important element of prevention is the patient taking responsibility for proper care of his diabetic feet. Because the patient is the first line of defense, education plays a crucial role in the prevention of diabetic foot problems. Patients must first understand the seriousness of the disease. Second, they must be educated that their first priority should be good control of their overall diabetic condition. Last, patients must learn the basics of good foot care and appropriate footwear.

Self care guide:

- Check your feet every day. Inspect the top, sides, soles, heels and between the toes.
- Wash your feet every day with lukewarm water and mild soap. Strong soaps may damage the skin.
- Test the temperature of the water before putting your feet in, because the normal ability to sense hot temperature is usually impaired in people with diabetes. Burns can easily occur.
- Gently and thoroughly dry the feet, particularly between the toes. Infections can develop in moist areas.
- Because of skin changes linked with diabetes, the feet may become very dry and may crack, possibly causing an infection. After bathing the feet, soften dry skin with lotion, petroleum jelly, lanolin, or oil. Do not put lotion between your toes.
- Soak your feet in lukewarm water to soften the nail before trimming. Cut the nail straight across, because curved nails are more likely to become ingrown.
- Exercise daily to promote good circulation. Avoid sitting with legs crossed or standing in one position for long periods of time.
- If you smoke, stop. It decreases blood flow to the feet.
- Wear shoes at all times to protect your feet from injury. Otherwise, if you have poor vision and less ability to feel pain, you may not notice minor cuts or bumps.
- Wear comfortable, well-fitting shoes. Never buy shoes that do not fit properly, expecting the shoes to stretch with time. Nerve damage may prevent you from being able to sense pressure from improperly fitting shoes.
- Check the inside of your shoes for rough areas or torn pieces that can cause irritation.
- Avoid wearing thong sandals or stockings with seams that can cause pressure points.
- Wear clean dry socks. Socks may provide an extra layer of protection between the shoe and your foot.
- Avoid using antiseptic solutions on your feet since these can burn and injure skin.
- Avoid applying a heating pad or hot water bottle to the feet. Avoid hot pavement or hot sandy beaches.

- Always feel inside footwear before you put them on (to check for stones, rough edges, etc).

- As a rule, the better the control of your diabetes, the less likely you are to develop complications such as foot ulcers.

- If obesity prevents you from being physically able to inspect your feet, ask a family member, neighbor, or visiting nurse to perform this important check.

- Also, where appropriate, treatment of high blood pressure, high cholesterol level and reducing any other 'risk factors' such as smoking, lack of exercise and obesity will reduce your risk of diabetes complications.

When to contact doctor:

Look for following symptoms which may require an immediate medical attention

- Persistent pain can be a symptom of sprain, strain, bruise, overuse, improperly fitting shoes, or underlying infection.

- Redness can be a sign of infection, especially when surrounding a wound, or of abnormal rubbing of shoes or socks.

- Swelling of the feet or legs can be a sign of underlying inflammation or infection, improperly fitting shoes, or poor venous circulation.

- Localized warmth can be a sign of infection or inflammation, perhaps from wounds that won't heal or that heal slowly.

- Any break in the skin is serious and can result from abnormal wear and tear, injury, or infection. Calluses and corns may be a sign of chronic trauma to the foot. Toenail fungus, athlete's foot and ingrown toenails may lead to more serious bacterial infections.

- Drainage of pus from a wound is usually a sign of infection. Persistent bloody drainage is also a sign of a potentially serious foot problem.

- A limp or difficulty walking can be sign of joint problems, serious infection, or improperly fitting shoes.

- Fever or chills in association with a wound on the foot can be a sign of a limb-threatening or life-threatening infection.

- Red streaking away from a wound or redness spreading out from a wound is a sign of a progressively worsening infection.

- New or lasting numbness in the feet or legs can be a sign of nerve damage from diabetes, which increases a persons risk for leg and foot problems.

An approach to a diabetic patient at primary health care center:

Prevention of ulcers starts with foot care screening for all patients who have diabetes. This entails a detailed history of foot care practices and physical examination of the feet for abnormal pressure sites, deformities, fungal infections and sensory and vascular examinations. The foot screening initial assessment has the goals of early recognition and prevention of minor injury to the foot, of identification of risk factors or current problems and of stratification of care. The initial history will take into account not only foot-related problems, but will also evaluate the active diagnoses, medications, allergies and social systems of tobacco use, levels of ambulation, educational level and support systems. The review of systems will also include

evaluation of the musculoskeletal, neurologic, vascular, ophthalmologic and skin integument. The history should include routine foot wear and foot care practices, such as how the patient resolves routine care of nails or calluses, what knowledge the person has regarding foot hydration or lubrication, if the person walks barefoot and what knowledge the person has regarding routine inspection for foot-related problems.

The foot examination will include assessment of the skin (texture, integrity, subcutaneous bruising), toenails (dystrophic or overgrown), calluses (on the plantar surfaces or between toes), signs of web space infections (fungal or tinea), ulcerations, skin bacterial infections (cellulitis), or infection within ulcers.

The musculoskeletal system should be evaluated looking at gait and any fixed or rigid deformities that will cause abnormal pressure distribution.

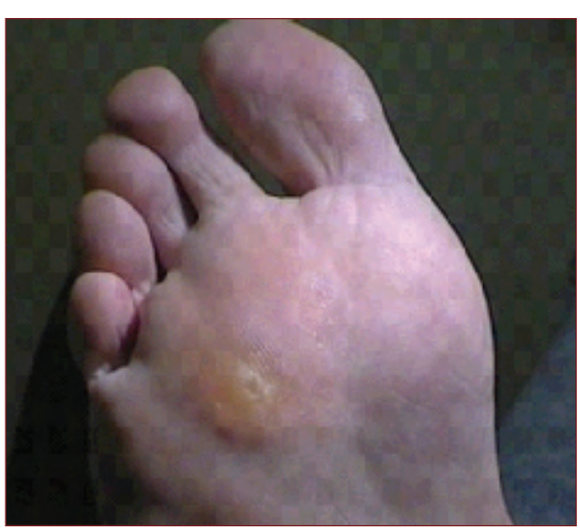
The neurologic component of the foot examination will include assessment of dorsiflexion and plantar flexion, strength and range of motion and plantar sensation with the use of the Semmes-Weinstein monofilament test (10 g), which tests for loss of protective sensation.

Footwear - The most common cause of foot injuries are shoes that are not properly fitted (too loose or too tight). In addition to examining the shoes worn to the clinic, inquiry should be made about other shoes worn. A fundamental part of prevention is to evaluate the footwear for the proper fit, the ability to protect the foot from trauma and the effects of the footwear on balance. The shape of the shoes should match the shape of the patient's feet. The patient who has loss of protective sensation often wears overly tight shoes to feel the shoe fit. Patients may be given a visual representation of the effect of an overly tight-fitting shoe by drawing the outline of a foot while they stand barefooted on a blank piece of paper. Comparison of the drawing of the foot with the shape of the shoe may emphasize to a patient areas of stress on the foot caused by pressure from the shoe. The shoes should be evaluated for the length and depth of the of the toe box.

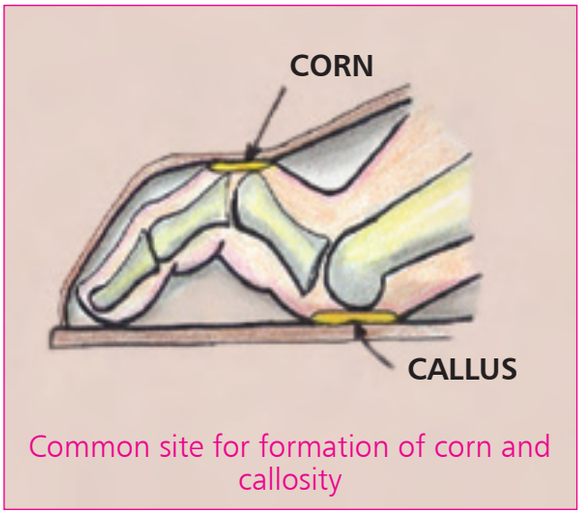
Socks - In addition to properly fitted shoes, choosing well-fitted socks may help protect against pressure and friction and also absorb moisture.

Skin - Patients should be advised to keep the spaces between their toes dry to prevent tinea pedis. Patients who have the loss of protective sensation in their feet may not sense these superficial infections and when unrecognized they may lead to maceration and ulceration. Tinea infections must be aggressively treated with topical antibiotics to avoid web space ulcerations.

Corns and calluses - Corns and calluses resulting from thinning fat pads, bony prominences and poorly fitted shoes may be precursors to ulceration.



Callosity on foot



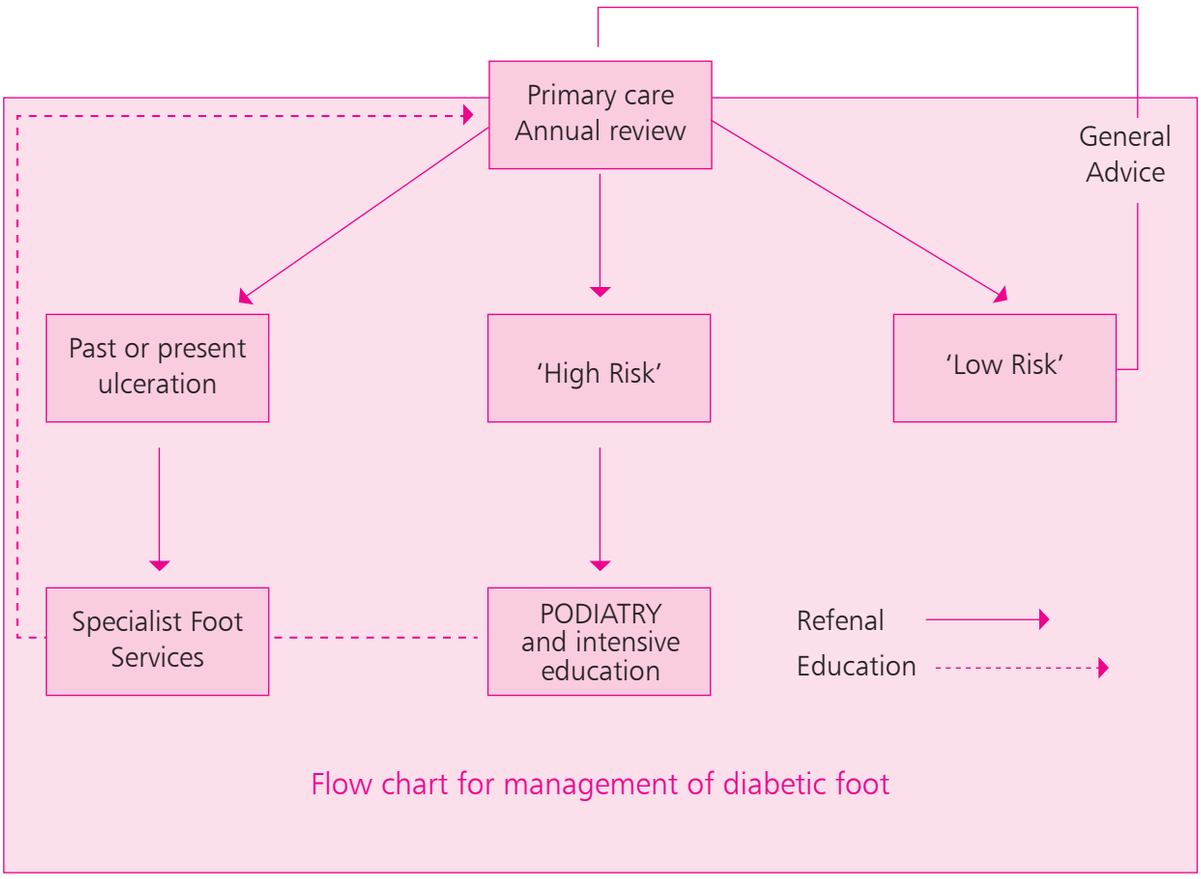
Common site for formation of corn and callosity

Musculoskeletal/gait - Elderly people who have fixed or rigid toes or foot deformities may have abnormal gait and balance. Reports of tripping or falling should be evaluated in the physical examination. Loss of dorsiflexion strength in the foot (foot drop) can lead to toe or foot drag during ambulation.

The patients who have loss of protective sensation, foot deformities, or peripheral vascular disease should be informed about their risk factors, re-educated at each visit. Shoes should be appropriately deep and wide.

Summary:

Foot complications in patients with diabetes mellitus are a challenge to the health care industry. A great deal of expenditure is due to the management of diabetic foot complications. This places a great burden on the health care industry. It also places a great burden on their families. Therefore, their effective management in an efficient manner is crucial to our patients. Intervention at the earliest possible time yields



Flow chart for management of diabetic foot

the best outcome. Prevention is the focus for those with no ulcerations. For those with ulcerations, prompt recognition and treatment is the key.

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Diabetes Mellitus and Anaesthesia

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Diabetes Mellitus is a clinical syndrome characterized by hyperglycemia due to absolute or relative deficiency of insulin. The overproduction or underproduction of hormones can have dramatic physiological and pharmacological consequences which severely affect the anaesthetic management.

Adults normally secrete 50U of insulin each day, which is the most important anabolic hormone and has multiple metabolic effects.

Metabolic effects:

- Increase in glucose and potassium entry into adipose tissues and muscle cells.
- Increase in glycogen, protein and fatty acid synthesis.
- Decrease in glycogenolysis, gluconeogenesis, ketogenesis, lipolysis and protein catabolism.

So lack of insulin is associated with catabolism and a negative nitrogen balance. These catabolic effects and other systemic end organ damage puts the anaesthetist at high levels of stress.

Diabetes mellitus

The number of people known to be diabetic is enormous and progressively increasing in the India and the World, which is fueled by the rise in Type2 diabetes caused by weight gain.

Diabetes has recently been reclassified into 4 types, type1 (insulin dependent), type2 (non insulin dependent) gestational diabetes and diabetes secondary to genetic defects.

There are three life threatening complications: Diabetic ketoacidosis, hyperosmolar non-ketotic coma and hypoglycemia increase preoperative morbidity and mortality.

Most of our diabetic patients are diagnosed prior to surgery

The aims of Preoperative assessment are:

- To know the Type of DM and its duration.
- Preoperative evaluation and treatment of end organ damage which is responsible for 5-fold increase in preoperative mortality associated with diabetes.
- Assessment of Blood sugar control.
- Quantification of risk

We do preanesthetic check-up in the Anaesthesia OPD.

A standard assessment is required with specific attention to the following systems for any type of diabetes.

1. Cardiovascular risk:

Long term complications of diabetes include coronary artery disease, hypertension, peripheral vascular disease, congestive heart failure, myocardial infarction, cardiomayopathy and cerebrovascular disease. We do routine ECG and if required the further assessment with 2D ECHO, TMT etc. These patients especially with autonomic neuropathy are more prone for 'silent ischemia' and 'sudden cardiac death'

in preoperative period. Chest radiograph may uncover cardiac enlargement, pulmonary congestion or plural effusion.

2. Respiratory:

Diabetics especially the obese and smokers are more prone for respiratory infections. Consider chest physiotherapy, humidified oxygen and bronchodilators in the postoperative period.

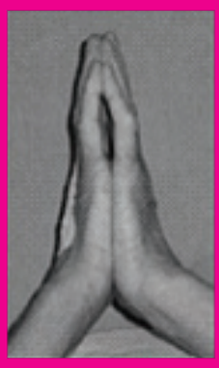
3. Airway:

Glycosylation of collagen in the joints leads to 'stiff joint syndrome', especially cervical and temporomandibular joints which can cause difficulty in intubation. Diagnosed by prayer's sign and cervical spine radiograph.

4. Renal:

Diabetes is one of the commonest causes of end-stage renal failure. Blood urea nitrogen, serum creatinine, serum electrolytes and if required, ABG should be checked for. Ensure adequate hydration to reduce postoperative renal dysfunction and renal failure. (7-9% incidence of postoperative renal failure)

The prayer sign



Patient is unable to approximate the palmer surfaces of the phalangel joints despite maximal efforts.

5. Central nervous system:

Anesthesiologists are more concerned with neuropathies. The types of neuropathies are: Autonomic neuropathy and Peripheral neuropathy.

Peripheral neuropathy:

The commonest is 'glove and stocking' type. Others are mononeuritis multiplex and painful sensory neuropathy. Documentation of preexisting neuropathy is prudent for:

Autonomic neuropathy:

Detecting autonomic neuropathy

Tests for autonomic neuropathy		Normal response	Abnormal response
Sympathetic System	Measure systolic blood pressure lying down then standing.	Decrease < 10 mm Hg	Decrease>30 mm Hg
Parasympathetic system	Measure heart rate response to deep breathing	Increase rate > 15 beats /min	Increase < 10 beats /min

Note: Positive tests indicate 1. Risk of unstable blood pressure myocardial ischemia, arrhythmias, gastric reflux and aspiration 2. Inability to compensate for intravascular volume changes, to maintain body temperature under anesthesia 3. Loss of signs of hypoglycemia, urinary retention and blunted response to atropine and beta-blockers.

- Medico legal issue especially if considering a regional technique of anaesthesia and

- Poor patient positioning during anaesthesia and transport of the patient is more likely to result in pressure sores that are often slow to heal.

6. Gastrointestinal:

Gastroparesis (delayed gastric emptying) and increased reflux of acid makes them more prone to regurgitation and at risk of aspiration on induction of anaesthesia.

Treatment is to follow proper nil by mouth (NBM) time, antacid and metoclopramide (increases gastric emptying).

7. Immune system:

Diabetics are more prone for infection. All invasive procedures should be performed under full aseptic precautions.

8. Eyes:

Diabetic retinopathy is common. Sudden rise in blood pressure should be taken care of to avoid rupture of retinal blood vessels which further damages the eyesight.

9. Miscellaneous:

Diabetes may be worsened by treatment with corticosteroids, thiazide diuretics and the contraceptive pills. Thyroid disease, obesity, pregnancy and even stress affect diabetic control.

10. Glucose control:

The best marker for recent control of blood sugar is the percentage of glycosylated hemoglobin (HbA1C). Levels less than 7% indicate good control whilst levels over 9% and particularly 12%, indicate poor control and likely associated with electrolyte and water loss and hyperglycemia in peri-operative period.

These patients should be admitted preoperatively for correction of these abnormalities and stabilization of blood sugar levels before the addition of surgical stressors.

The Goal is; FBS 80-120mg/dl and PLBS- 100-140mg/dl

Anesthetic management goals:

1. To maintain glycemic control-

Tight glycemic control especially in patients for cardiopulmonary bypass, with global CNS damage, pregnant patients (improve fetal outcome) and those requiring postoperative ICU care. Aim is 80 to 120mg/dl.

Non tight glycemic control – Aim for blood sugar level between 150-200mg/dl.

The Primary goal of intra-operative blood sugar management is to avoid hypoglycemia which if untreated leads to irreversible cerebral damage, especially during general anaesthesia.

Avoid hyperglycemia (>180mg/dl) which carries risk of hyperosmolality, infection and poor wound healing.

2. To avoid further deterioration of pre-existing end organ damage.

3. To start drugs for glycaemic control as soon as possible.

Anaesthetic management:

The preoperative orders include:

- Consent
- NBM orders

- Anxiolytic agent
- Aspiration prophylaxis
- Stop long acting insulin/OHA night before surgery
- No insulin/Oral Hypoglycemic Agent on morning of surgery
- Morning sample of blood sugar, serum electrolytes and ECG
- Monitoring IV fluids according to regimen
- To arrange for dextrostix, insulin etc.
- Careful transfer of patient
- To be taken up as 1st case.

Timing - Diabetic patients should be placed first on the operating list to shorten the preoperative fast and potentially allow normal oral intake later that same day.

Diabetes and stress

Surgery is a physical stress characterized by catabolism, increased metabolic rate, increased protein and fat breakdown, negative nitrogen balance, starvation and glucose intolerance. The degree of stress will be related to factors such as operation length, type of procedure and the presence of any complications such as infection.

All of these metabolic effects are exaggerated in the diabetic, particularly where there is a virtual absence of endogenous insulin. The pronounced catabolism results in fatty acid production, ketogenesis and hyperglycemia and eventually to ketosis or ketoacidosis.

Medications – Continue all diabetic medication until the day of surgery except:

a. Chlorpropamide (stop 3 days prior as long acting, substitute with a shorter acting sulphonylurea)

b. Metformin During major surgery metformin is avoided as there is a risk of lactic acidosis and is restarted if renal and hepatic functions remain adequate.

c.) Glitazones

c. Long acting insulin Substitute with short/ intermediate acting.

If the patient is expected to eat within 4 to 6 hours of the operation, then treat this group as having "Minor" surgery. Otherwise, surgery is "Major".

The perioperative glycemic management is adjusted according to:

- The extent of the anticipated surgery
- Whether the patient is insulin dependant (IDDM) or non-insulin dependant (NIDDM)

Note: Distinction between Type1 and Type2 diabetes is important for deciding a peri-operative glycemic management plan. Since Type1 are absolutely deficient in insulin, they require it all the time to avoid catabolic state of ketoacidosis.

- Whether the surgery is elective or emergency.

Note: elective cases are to be performed with well controlled diabetes.

- Emergency cases (except dire emergency e.g. torrential bleeding, complete airway obstruction) should be taken in optimized condition (Most of the diabetic emergency cases come with either hyperglycemia or diabetic ketoacidosis for surgery).

Protocols for glycemic control on the day of surgery

A large number of protocols exist for managing insulin and glucose requirement in the diabetes.

The protocols which we follow are-

For patients on OHA:

- Omit morning dose of OHA. Blood sugar on table before starting the case.
- For minor surgical procedures avoid glucose containing solutions. Avoid lactated ringer's solution which may predispose to hyperglycemia, as lactate is converted to glucose.
- Based on blood sugar determinations, regular insulin is used to treat hyperglycemia intra and postoperatively.

Note: The effects of OHAs of short duration of action may be prolonged in renal failure.

- For major surgeries OHAs are converted to regular or intermediate insulin and treated as follows.

For patients who are on insulin or converted to insulin:

- Omit the morning dose of insulin.
- Blood sugar on table before starting the case and every 1 to 2 hours or more frequently if required.
- Glucose as a continuous infusion of 100 to 125ml/hr as a 5% Dextrose solution. (When the patient is not expected to resume oral intake for a few days, intravenous glucose acts as a substrate for the increased metabolic demand, thus providing a protein-sparing effect).
- Continuous infusion of insulin adjusted according to the formula

$$\text{Insulin (U/hr)} = \frac{\text{Plasma Glucose (mg/dl)}}{150}$$

(Note: The denominator should be 100 if the patient is taking corticosteroids e.g. 10mg of prednisolone a day or its equivalent, not to include inhaled steroids)

- If sugars are very high >250mg/dl, small doses of insulin 1to2U can be given as intravenous boluses along with continuous infusion.
- One unit of regular insulin given to adult lowers plasma glucose by 25to30 mg/dl (may not apply in catabolic states, such as sepsis).

The keystone to intraoperative diabetes management is the measurement of blood glucose concentration. Since individual insulin needs can vary dramatically, any formula can be considered as a guideline.

Note: A patient who takes NPH or protamine zinc insulin is at increased risk for allergic reactions to protamine sulphate- including anaphylactic shock and death. Caution to be taken during heparin reversal of CP-Bypass. Protamine test dose of 1 to 5 mg is given 5 to 10 minutes prior to full reversal.

After delivery of placenta the insulin requirement decreases.

Postoperatively – In patients, who are insulin controlled, stop the infusion when eating and drinking. Adjust the daily subcutaneous insulin according to blood sugar level. If OHA controlled,

stop infusion and restart oral hypoglycemic once patient starts eating. Close monitoring of the diabetic's blood sugar must continue postoperatively. This is because of the progression of stress period in postoperative period.

Anesthetic techniques:

The type of anaesthesia depends on the site and type of surgery. As far as possible, regional anaesthesia is preferred over general anaesthesia.

General Anaesthesia

If gastric stasis is suspected then a rapid sequence induction is used. A nasogastric tube can be used to empty the stomach and allow a safer awakening.

May face with difficulty in intubation

IV induction agents normally cause hypotension on injection due to vasodilatation. If a patient has a damaged autonomic nervous system (and many diabetics do), then they cannot compensate by vasoconstriction, and the hypotension is worsened. Reducing the dose of drug and giving it slowly helps to minimize this effect.

As such the metabolic effects of modern anesthetics are minor as compared with the stress of surgery during both general and regional anaesthesia.

Hypoglycemia is a major complication during general anaesthesia and can be avoided by frequent measurement of blood glucose level.

Hypoglycemia (blood glucose less than 60mg/dl) is one of the main dangers to patients in the peri-operative period.

The usual warning symptoms and signs in the awake patient include profuse sweating, pallor, light-headedness, tachycardia, confusion and incomprehensible speech progressing to convulsions and coma.

Hypoglycemia if untreated causes irreversible brain damage.

Liver disease, fasting and sepsis exacerbate hypoglycemia.

Hypoglycemia may also result inadvertently by poor blood glucose monitoring or equipment failure.

The best warning signs and symptoms of hypoglycemia seen in concious patient, are lost under general anaesthesia.

Frequent monitoring of blood glucose and appropriate adjustments to therapy is the key in prevention of hypoglycemia during general anaesthesia.

Once detected, give 25ml of 50% dextrose intravenously and repeat if blood sugar measurement doesn't increase (each ml of 50% glucose will raise the blood glucose of a 70kg adult approximately by 2mg/dl).

Regional techniques

Regional techniques of anaesthesia in diabetics offer some potential advantages such as.

The avoidance of intubation having patient awake to warn of impending hypoglycemia.

Earlier return to normal eating patterns.

Document any existing motor/sensory neuropathies prior to performing any blocks and look for evidence of autonomic neuropathy. If present, expect increased hypotension after neuraxial blocks.

Note: Local Anesthetics with Adrenaline should strictly be avoided.

Intraoperative monitoring

Blood sugar monitoring is most important every 1 or 2 hours. Monitor blood pressure and pulse every 5 minutes, ECG, SpO2 and EtCO2 during the operation, and watch skin colour and temperature. If the patient is cold and sweaty, then suspect hypoglycemia, check the blood glucose STAT.

Diabetic outpatients (day care surgery) may require admission to the hospital overnight if persistent nausea and vomiting from gastroparesis prevent oral intake.

Diabetic versus Non-diabetic – Diabetes itself may not be as important to preoperative outcome as its end-organ effects. Sepsis and complications of atherosclerosis are the leading causes of death in these patients. Other changes such as autonomic neuropathy contribute to increased morbidity. Episodes of hypo and hyperglycemia and diabetic ketoacidosis, conditions not encountered in the healthy population, carry a higher than normal risk of perioperative morbidity.

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The Problem With Diabetes

- >200 million people worldwide
- 380 million in 20 years time !
- 3.8 million deaths / year
- 46% in the 40-59 age group
- 13-20% of people > 65 yr have DM

Diabetic Retinopathy

Dr. S.U. Nadkarni
Medical Officer
Department of Ophthalmology

Introduction

Diabetic retinopathy is the most common diabetic eye disease and a leading cause of blindness in adults. It is caused by changes in the blood vessels of the retina.

In some people with diabetic retinopathy, blood vessels may swell and leak fluid. In other people, abnormal new blood vessels grow on the surface of the retina. The retina is the light-sensitive tissue at the back of the eye. A healthy retina is necessary for good vision.

If one has diabetic retinopathy, initially one may not notice changes in vision, but with time, diabetic retinopathy can get worse and cause vision loss. Diabetic retinopathy usually affects both eyes.

Stages of Diabetic Retinopathy:

1.Mild Nonproliferative Retinopathy:

Microaneurysms are seen. They are small areas of balloon-like swelling in the retina's tiny blood vessels.

2. Moderate Nonproliferative Retinopathy:

As the disease progresses, some blood vessels that nourish the retina are blocked.

3. Severe Nonproliferative Retinopathy:

Many more blood vessels are blocked, depriving several areas of the retina of their blood supply. These areas of the retina send signals to the body to grow new blood vessels for nourishment.

4. Proliferative Retinopathy:

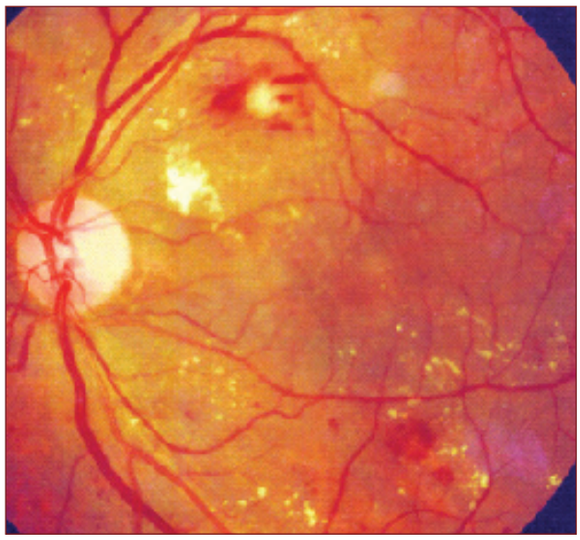

Fig.1 - Diabetic retinopathy (proliferative)

(FIG.I) (FIG.4) At this advanced stage, the signals sent by the retina for nourishment trigger the growth of new blood vessels. This condition is called proliferative retinopathy. These new formed blood vessels are abnormal and fragile. They grow along the retina and along the surface of the clear, vitreous gel that fills the inside of the eye. (FIG.2) They have thin, fragile walls and if they leak blood, there can be vitreous haemorrhage.

All people with type 1 and type 2 DM are at risk. Therefore each and everyone with diabetes should get a comprehensive dilated eye examination annually. The longer the history of diabetes, the greater the chances of getting diabetic retinopathy. Between 40 to 45 percent of patients diagnosed with diabetes have some stage of diabetic retinopathy. If a patient has

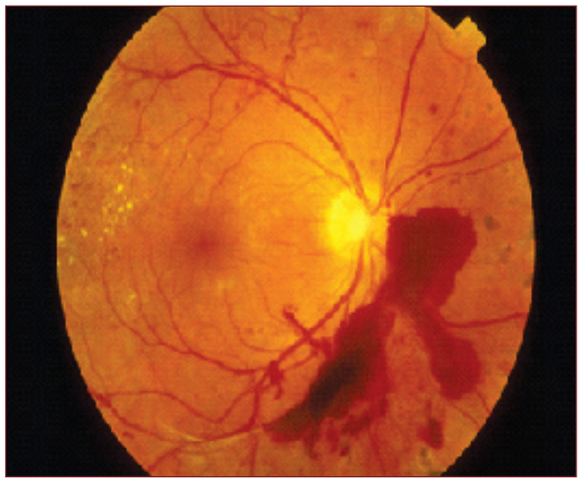

Fig.2 - Vitreous heamorrhage

diabetic retinopathy, the doctor can recommend treatment to help prevent its progression.

Diabetic retinopathy may be a problem for diabetic women during pregnancy. To protect vision, every pregnant woman with diabetes should have a comprehensive dilated eye examination as soon as possible. The doctor may recommend additional examination during pregnancy.

If a patient has diabetes he/she should get a comprehensive dilated eye exam at least once a year. Proliferative retinopathy can develope without symptoms. At this advanced stage, one is at high risk for vision loss. Macular edema can develop without symptoms at any of the four stages of diabetic retinopathy. (FIG.3)

- Visual acuity test.
- Dilated eye examination.
- Tonometry – for measuring intraocular pressure.
- Fluorescein Angiogram for identifying any leaking blood vessels.

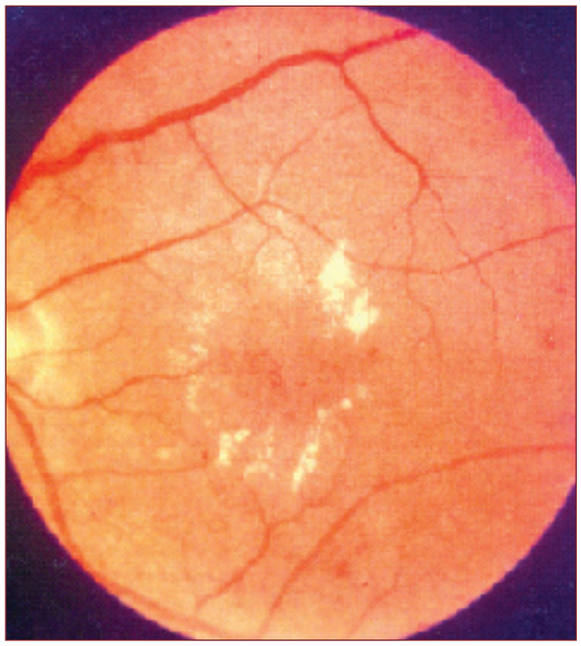

Fig.3 - Diabetic maculopathy

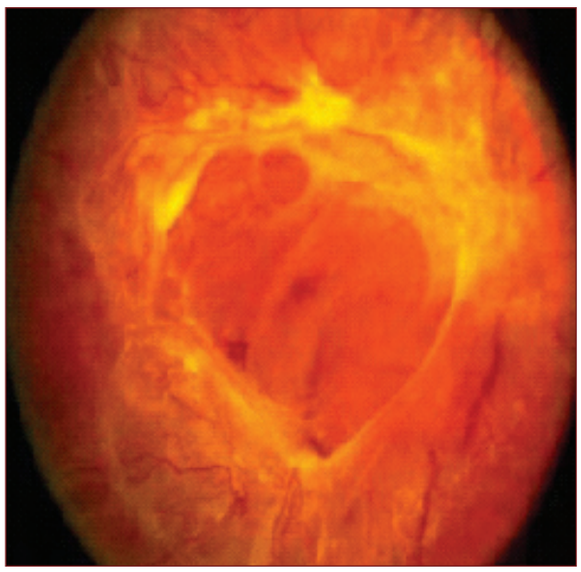

Fig.4 - Proliferative retinopathy (fibrovascular)

Management:

- Early Stages – Needs control of blood sugar, cholesterol levels and blood pressure.
- Regular screening.

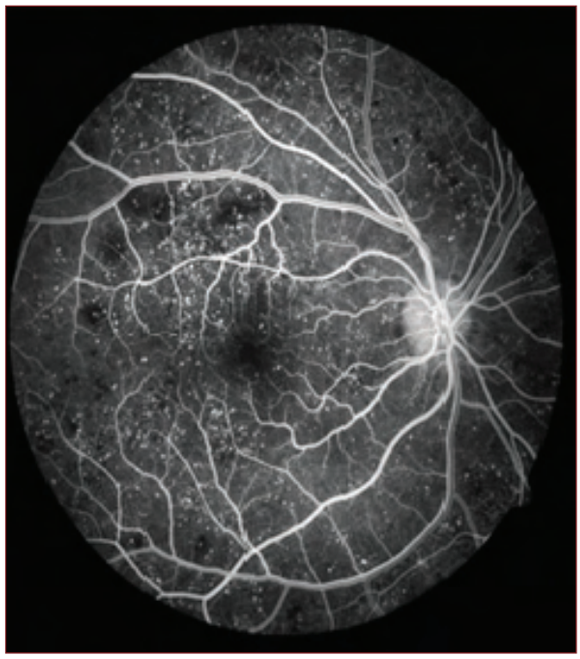

Fig.5 - Fluorescein angiography

Surgical treatment:

- Treatment by laser- photocoagulation-it is best in preventing vision loss and reducer risk of blindness by 60-90% in leaking and abnormal new blood-vessels.

- Vitrectomy- This is advanced surgery in cases of blood accumulation in vitreous-gel.

- Low vision counscelling – Low vision services and devices may help the patient to make the most of the remaining vision.

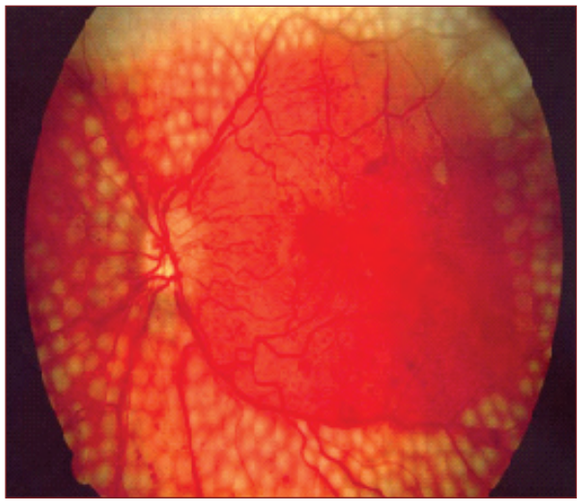

Fig.6 - Laser photocoagulation

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Diabetes Polypill - SAMTA Pill

- **S**tatin
- **A**spirin
- **M**etformin
- **T**hiazide
- **A**CE-I or ARB

Indo-linguistically: "equality" ie in terms of reducing morbidity and mortality esp. CVD

A Little about Insulin

Dr. A.R. Kulkarni, Medical Officer
Dr. Mihir Raut, Resident Medical Officer
Department of Medicine

Introduction

Mankind knows Diabetes Mellitus since centuries. Indian medical history mentions madhumeha in Charak Samhita (500 -700 BC) and has given description of disorder in detail. Charak mentioned that the madhumehi person passes large amount of sweet urine.

Glucose is essential for providing energy for normal body functions. In diabetes the blood glucose level increases due to relative or absolute deficiency of insulin. Insulin acts as a gatekeeper that regulates the entry of glucose into the cell.

There are misconceptions in the minds of people about insulin treatment. Just a prescription of insulin does not mean that the disease is severe. Any type of Diabetes Mellitus is a major illness. It needs to be treated with whatever possible means. The fear of insulin is due to its mode of delivery which is through injection. But with newer types of injection syringes and with right

Classification of Insulins: Insulins can be classified as short-acting or long-acting. (As per table below)

Pharmacokinetics of Insulin Preparations

	Time of Action		
Preparation	Onset, h	Peak, h	Effective Duration, h
Short-acting, sbcutaneous			
Lispro	<0.25	0.5-1.5	3-4
Aspart	<0.25	0.5-1.5	3-4
Glulisine	<0.25	0.5-1.5	3-4
Regular	0.5-1.0	2-3	4-6
Short-acting, inhaled			
Inhaled regular insulin	<0.25	0.5-1.5	4-6
Long-acting			
NPH	1-4	6-10	10-16
Detemir	1-4	_a	12-20
Glargine	1-4	_a	24
Insulin Combinations			
75/25-70% protamine lispro, 25% lispro	<0.25	1.5h[b]	Up to 10-16
70/30-70% protamine aspart, 30% aspart	<0.25	1.5h[b]	Up to 10-16
50/50-50% protamine lispro, 50% lispro	<0.25	1.5h[b]	Up to 10-16
70/30-70% NPH, 30% regular insulin	0.5-1	Dual	10-16
50/50-50% NPH, 50% regular insulin	0.5-1	Dual	10-16

technique one experiences minimum pain while taking the injection.

Most of the current insulin preparations are generated by recombinant DNA technology and consist of the amino acid sequence of human insulin or variation thereof for example one short-acting insulin formulation, insulin lispro, is an insulin analogue in which the 28th and 29th amino acids (lysine and proline) on the insulin B chain have been reversed by recombinant DNA technology. Insulin aspart and insulin glulisine are other genetically modified insulin analogues with properties similar to insulin lispro. Insulin aspart, lispro, or glulisine is preferred over regular insulin for prandial coverage.

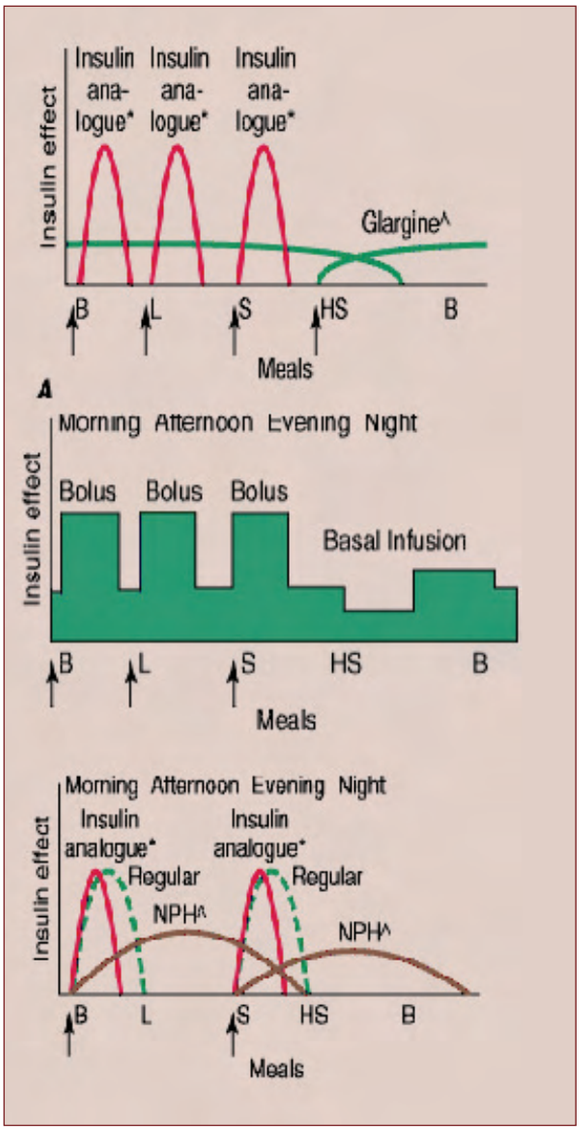
Insulin glargine is a long-acting biosynthetic human insulin that differs from normal insulin in that asparagine is replaced by glycine at amino acid 21, and two arginine residues are added to the C-terminus of the B chain. Compared to NPH insulin, the onset of insulin glargine action is later, the duration of action is longer (~24 h), and there is no pronounced peak. A lower incidence of hypoglycemia, especially at night, has been reported with insulin glargine when compared to NPH insulin.

Sites for insulin injection:

Insulin injections are easy to take.
The usual injection sites for self injection are:

- Abdomen -The most preferred site because of its faster and uniform absorption and because it is least affected by exercise
- Front and outer area of the thighs- avoid inner aspect of the thigh
- Buttocks
- Lateral aspects of arms

Representations of various insulin regimens



Injection sites over thighs:

Lower Border	3 Fingers above knee joint
Upper Border	3 Fingers below groin fold
Inner Border	Middle of thigh
Outer Border	Groove on outer aspects of thigh

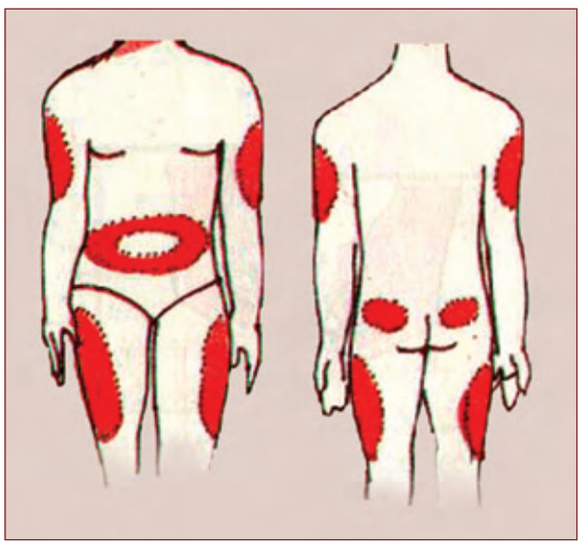
Injection site over abdomen:

Lower Border	Two fingers above groin fold
Upper Border	Two fingers below lower rib
Inner Border	Two fingers outer to umbilicus
Outer Border	Four fingers away from inner line

Draw two rectangles on outer aspects of umbilicus (Navel)

Following picture depicts various sites where injection can be taken.

Injection can be taken in areas marked red Insulin is needed by



1. Young diabetics
2. Very high blood sugar levels
3. Pregnant diabetic women
4. Diabetics who have to undergo operative procedures and/or other serious illness.
5. Diabetics with associated complications like heart or kidney disease may require insulin in addition to oral tablets.
6. With infections like tuberculosis or hepatitis in presence of diabetes, one should not hesitate to start insulin.

Insulin preservation

Storage of insulin is very important for its best action. Insulin should be stored preferably in fridge (on the door at the bottom level). It should not be frozen. It should not be exposed to extreme temperatures like shelves near the cooking stove in the kitchen or geysers in the bathroom. Constant sunlight at the windows can cause a problem if the bottle of insulin is left there. Insulin can be kept for 15-30 days at room temperature also.

Insulin and travel (Precautions)

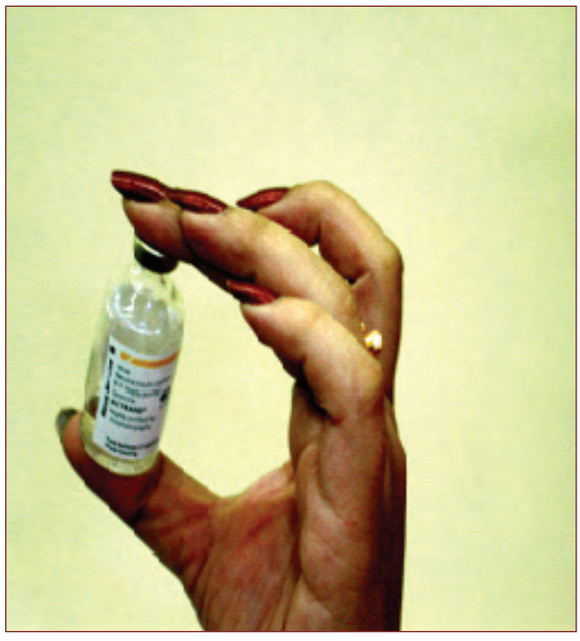
- Please do not store insulin vials along with hot lunch box.
- Carry enough stock of insulin vials, syringes, needles and spirit swabs.
- Carry your glucometer with enough strips.
- Carry sweets /chocolates for hypoglycemia management.
- Carry prescriptions for insulin and syringes.

Injection technique:

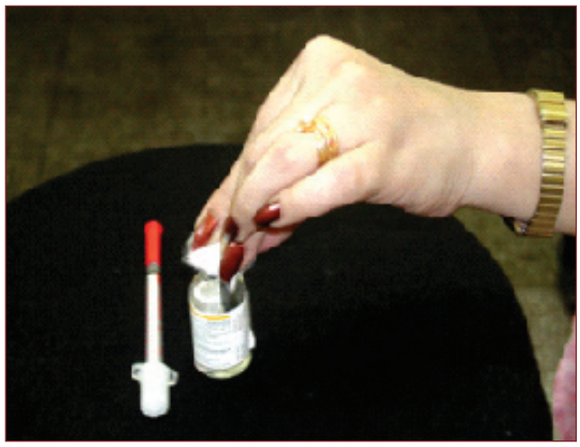
How to prepare insulin shot?

Wash your hands thoroughly. Roll the insulin vial in both hands. Do not shake it.

Take cloudy insulin or intermediate acting insulin vial. Clean the top with spirit swab.



Insert the needle in the vial and push air inside the vial, amount equal to units of insulin you are required to take. Take out empty syringe without any insulin in it. Now take vial of clear or rapid acting insulin. Push air inside the vial, amount equal to units of your insulin dose. Turn vial-syringe unit upside down. Just pull back the plunger to withdraw clear insulin. Take out the needle.



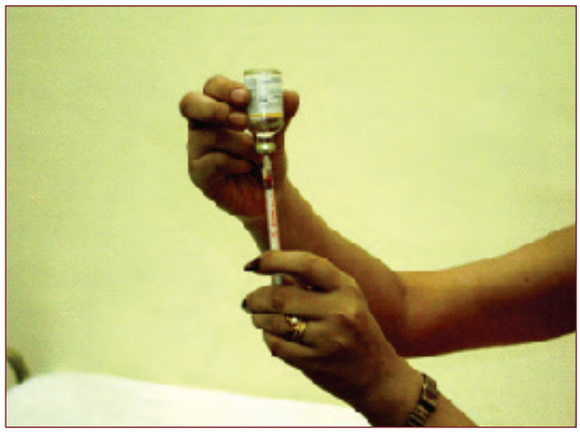
Now insert needle in the cloudy insulin vial. Pull the piston back so that insulin flows inside the syringe without getting mixed inside the vial. Remove air bubbles by firmly flicking the syringe.

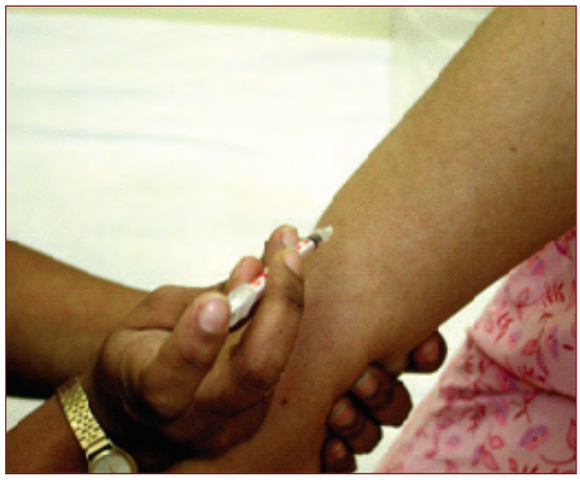
You are now ready for the insulin shot.

Clean the area where you want to inject. Pinch the fold. Hold syringe like a pen with thumb and middle finger. Press the plunger with index finger, straight in the skinfold. You have injected successfully.

Injection device

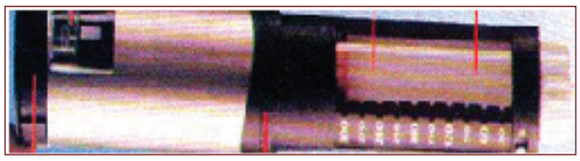
Insulin syringes that are available in markets are disposable and capable of offering near "painfree" injections. Insulin portable pens, insulin jets and portable insulin pumps are also available.





Insulin pen

The pen-like instruments are now available in the market, which allow you to dial your dose and inject. These pens have following features:



They assure a freedom from syringes. They are very accurate; less painful. They increase the self confidence of the patients and assure them of a near normal social life.

"Dial & inject" helps the visually impaired and elderly patients.

References:

1. Textbook of Diabetes Mellitus RSSDI (Research Society for the Study of Diabetes in India) vol.3.

2. Harrison's Principles of Internal Medicine 17th edition.

Alphabet Diabetes Care Strategy

Advice:
Blood Pressure:
Cholesterol:
Diabetes Control:
Eyes:
Feet:
Guardian Drugs

Frequently Asked Questions about Diabetes

Dr. Sanjay Kanoje,
Dr. Chitra Bongirwar
Medical Officers
Deonar (E) Dispensary

Diabetes mellitus affects millions of people worldwide according to the current estimates from the World Health Organization. This dreaded disease is a major cause of death and can cause some complications that can make life miserable for those affected. However, many of these deaths and complications can be avoided if people knew a bit more about diabetes and how to handle it. In this section, you will learn a lot about diabetes mellitus. The information provided will help you cope with diabetes or help you understand what a diabetic patient has to cope with.

What is diabetes?

Diabetes mellitus is a chronic disorder in which the body's ability to use sugars is reduced. This can cause raised levels of glucose in the blood and its excretion in the urine. These changes are the result of a deficiency of the pancreatic hormone, insulin. There are two main types of diabetes: type 1 or insulin-dependent diabetes mellitus (IDDM), and type 2 formerly known as non-insulin-dependent diabetes mellitus (NIDDM). Diabetes can also be diagnosed during a pregnancy and when due to the extra demands of the pregnancy is called gestational diabetes.

What is type 1 and type 2 diabetes, how do they differ?

This division is important because it affects the subsequent treatment. The mechanisms of the two differ, though they both result in an inability to regulate glucose properly.

Type 1: This form has a sudden onset (at most a few weeks), usually before the age of 40, but can occur at any age. The beta cells in the pancreas which produce insulin are killed off by the person's own body. Insulin treatment is essential for life and will always have to be taken. Without insulin, blood glucose levels become too high and fat is broken down as an alternative source of energy. This results in the production of ketone bodies which, if they accumulate, can lead to ketoacidosis. This in turn can cause nausea, vomiting and drowsiness, and can lead to diabetic coma. Insulin is currently given by injection or pump.

Type 2: This is the form that most people with diabetes have. It affects mostly people over the age of 40 and has a slow onset (years) that may go undiagnosed. People with type 2 diabetes still secrete insulin, though there is almost always some reduction in the quantity produced.

Although type 1 and type 2 are clinically distinct from each other, many people with type 2 may develop a need for insulin injections in order to manage their diabetes effectively.

What are the symptoms of diabetes?

The 'classical' symptoms of both types of diabetes are thirst, tiredness, itching or rash in the genital areas caused by yeast-like infections of glucose-rich urine, over-production of urine (especially at night) and weight loss. In type 1, less frequent symptoms are cramps, constipation, blurred vision, and skin infections. In type 2 diabetes, the onset of symptoms may be so gradual that

they go unnoticed. People with type 2 diabetes who have remained undiagnosed for some years may eventually be diagnosed because they go to the doctor complaining of deteriorating eyesight or with foot ulcers or pain in the limbs, which are some of the signs of complications of diabetes.

How do I know I have Diabetes?

At the beginning there may not be any symptom. When blood sugar is above 180 mg%, sugar starts appearing in the urine. Sugar in the urine drags water and you pass a lot of urine and feel dry and thirsty. You may also feel tired and loose weight. Your appetite increases and peculiarly you may notice that you are loosing weight in spite of eating more. Chance of infection is higher if you have high sugar and also your healing from infection, cut or wound may be unusually delayed. Some people complain of poor eyesight.

Who are at risk of Diabetes?

Family history of Diabetes is the major risk factor. Sedentary life-style, obesity, smoking, excessive alcohol intake, high blood pressure and in case of women previous Diabetes in pregnancy or delivering big baby (birth weight more than 4Kg) are risk factors.

Can I prevent Diabetes when my risk is high?

If you have family history, you cannot do anything about that. Things in your hands are healthy eating (i.e., eating vegetables and fruits, avoiding fast food), healthy life-style (regular exercise, avoidance of smoking, moderation of alcohol, etc) and keeping your weight in accordance to your height. Certain medicines are being used recently for preventing Diabetes in people who have borderline Diabetes.

I have nobody in my whole family with Diabetes, how did I get it then?

Family history certainly is an important factor, we all have high-risk gene for Diabetes. Remember it is not your fault that you have Diabetes. You are just happened to be the person who got it. In India 4% of villagers and up to 15% of city dwellers have Diabetes. Not only have we more Diabetes, but we get it at an earlier age than people in the west (about 10 yrs earlier).

Do I need to stop eating out?

Certainly not, as long as you are not planning to eat out everyday! You need to know what the right food is and the correct amount.

Can I have ice cream?

Occasionally yes, but do not make a habit of eating ice cream regularly. There are certain ice cream available now with no added sugar, but do not forget they have calories.

What is insulin?

Insulin is a hormone produced by our bodies, specifically our pancreas. Among its many functions, insulin helps with the movement of glucose from the blood into body cells where glucose is used as a source of energy or stored as a fuel source. Without insulin, body cells can "starve", even though there may be plenty of glucose in the bloodstream.

What is hypoglycemia (low blood sugar) ?

Hypoglycemia occurs when there is an imbalance between insulin and glucagon. Glucagon is a hormone produced by our bodies that raises the level of glucose in the blood, and is an important factor in hypoglycemia. To keep diabetes under control, it is important to test your blood glucose frequently. Good diabetes control, including an appropriate diet, is the best way to prevent hypoglycemia.

How I know that I am hypoglycemic?

Some of the important symptoms of hypoglycemia are as follows:

- Hunger
- Sweating and trembling
- Blurred vision
- Head ache
- Dizziness

If you take insulin or a diabetes pill that can cause hypoglycemia, always carry some sweets for emergencies.

Now that I have been diagnosed with diabetes, do I have to give up all the foods that I love?

While you may have to adjust your serving sizes and how often you eat them, most foods can fit into your eating plan. The key to following a healthy diet is moderation, which everyone, whether they are diabetic or not, should follow. Consult with your dietitian to help you develop your own personalized healthy eating plan.

Do I have to completely eliminate sugar from my diet?

People with diabetes can fit sweets into their meal plan by substituting for other carbohydrate foods, It's the total amount of food and type of food consumed that really matters. Consult your registered dietitian to find out what is the right amount for you.

Should I try to eat at the same time each day?

It is helpful to have a regular eating schedule. This will help keep your blood glucose level better balanced. Also, don't miss out on breakfast.

Did I get diabetes because I ate too much sugar?

Eating too much sugar is not a good thing, but it doesn't cause diabetes. Eating too many calories and not getting enough exercise can lead to being overweight, however, which has been found to be a leading contributor to developing type 2 diabetes.

Since I'm taking insulin, does that mean I can eat anything I want?

The pills or insulin shots are more effective when they don't have to work as hard to lower your blood glucose levels. Combining your medication with a healthy diet and exercise program will give you the best results.

What are some good types of exercise for people with diabetes?

There are many different forms of aerobic exercise that are appropriate for people with diabetes, including walking, swimming, dancing, aerobics, basketball, and tennis. Be sure to consult with your physician before you begin any exercise routine. You can also add physical activity to your daily routine by walking or riding your bicycle instead of driving, doing housework, gardening, or walking the dog, for example.

Will menopause affect my diabetes?

Yes. The changes in hormonal levels and balance, may lead to BG levels that are out of control. Women with diabetes are also at risk of developing premature menopause and consequent increased risks of cardiovascular disease.

Can women with diabetes breastfeed their babies?

Unless advised otherwise, yes. Breast milk provides the best nutrition for babies and

breastfeeding is recommended for all mothers with either preexisting diabetes or gestational diabetes.

I had gestational diabetes. How soon after having the baby should I get my blood glucose rechecked?

About 6-8 weeks after delivery. Like 90% of the women with gestational diabetes, your BG levels will probably return to normal right after your baby is born. However, you still run the risk of developing type 2 diabetes. In fact, 5% of women with gestational diabetes will have type 2 diabetes and 15% will have pre-diabetes by the time of this first screening.

Will my children inherit diabetes from me?

It all depends on risk factors that include: no diabetes in the family — 11% chance of type 2 diabetes by age 70 and 1% chance of type 1 diabetes by age 50. One parent with type 1 diabetes — 6% chance of type 1 diabetes (father with type 1 diabetes), 4% chance of type 1 diabetes (mother with diabetes who was younger that 25 when the child was born) and 1% chance of type 1 diabetes (mother with diabetes who was older than 25 when the child was born). *Risk doubles if the parent was diagnosed by age 11*

One parent with type 2 diabetes (diagnosed before the age of 50) - 14% chance of type 2 diabetes.

Both parents with type 2 diabetes (overall risk) - 45% chance of type 2 diabetes.

Does eating a lot of sugar really cause diabetes?

No. People who eat foods high in sugar are at risk of gaining weight because sugar adds calories. Being overweight is associated with developing Type 2 diabetes, but eating sugar does not cause diabetes.

If I take my diabetes medication (insulin or pills), do I have to watch my diet?

Unfortunately, medication alone cannot adequately control blood glucose levels and keep you in the best of health. Eating appropriate foods at regular meal times is an important part of diabetes management and control.

I've heard that diabetes skips a generation. Is that true?

No. Unfortunately, people who have a parent with diabetes are actually at higher risk for developing the disease than people with no family history of diabetes.

Are the pills I'm taking insulin?

No. Currently, insulin only comes in an injectable form. Experiments with pill forms have shown that our saliva and stomach acid damages the insulin and decreases its effectiveness. Diabetes pills help your body produce more insulin or use your own insulin more effectively, but they do not contain insulin.

How is the diagnosis confirmed?

To be sure that someone has diabetes, a blood glucose test needs to be done. There are 2 common tests. One done when you have not eaten for 6 hours called the Fasting blood glucose. And the second is taken 2 hours after eating a meal. This is called a 2 hour post prandial glucose.

There are other means of estimating the level of blood glucose but are not as accurate. A good example is a urine glucose test. Please note that there is a difference between the blood glucose values and plasma glucose values.

What are the complications of Diabetes?

The common complications of diabetes include blindness, foot gangrene leading to

amputation, sexual dysfunction, kidney disease, and cardiovascular problems. Most of these complications can be avoided or delayed if proper treatment is started early.

What are the early and late complications of Diabetes?

Uncontrolled Diabetes can give rise to many complications. These are either Acute or Short term and Chronic or Long term.

Acute (early) problems are due to either low blood sugar causing Hypoglycemia or High Blood Sugar causing Hyperglycemia or Diabetes Ketoacidosis.

Chronic (Late) complication associated with Diabetes are High Blood Pressure and Heart problem leading to Heart Attacks and Heart Failure, difficulty in vision and Eye problem leading to Blindness, Kidney problem leading to Kidney Failure, Nerve damage primarily leading to problem of the Foot but also to problem such as Diarrhoea, Constipation, Nausea, Vomiting etc, arising from damage to Nerves in other parts of the body.

How is Diabetes treated?

At the moment there is no cure for diabetes. However it can be treated by making sure that the glucose in the blood stays within the normal limits. The main treatment options being used today include Lifestyle modifications such as eating healthy diets and exercise and weight loss programs modifications.

Insulin injections and the new insulin inhalers and Diabetic pills, Other forms of treatment being developed include islet cell transplants, pancreatic transplants etc.

What is an insulin pen?

This is a device by which insulin can be administered without much pain. It also does not require storage in refrigerator and can be carried easily. Insulin pen is becoming more popular nowadays.

What is meant by insulin allergy?

Some patients who are taking insulin may develop allergy to insulin. The patient may have fever, cough, skin rashes etc. If any of these things occur, the patient should reach the hospital immediately. However, nowadays due to the availability of newer insulin preparations, allergy is not common.

Which is the best method to test diabetes? Urine or blood glucose?

Urine test for glucose will be positive only if the blood glucose is above 180 mg%. Hence it is not the accurate method. Blood tests measures the exact level of glucose and hence it is the most accurate method.

I don't have a refrigerator in my house. How can I store insulin?

It is not essential to store insulin in fridge. Ideal storage conditions can be maintained even by keeping it in a glass of water.

Can I stop medicines when my diabetes is controlled?

In most of the cases diabetic patients require medicines throughout the life. Hence you should never stop the medicines even after blood glucose is controlled. Always take medicines according to the doctor's advice.

What is an HbA1C?

All parts of your body including your red blood cells rely on glucose for energy. When glucose enters your red blood cell it bonds with oxygen carrying hemoglobin to form hemoglobin A1C. (HbA1C). The higher the blood glucose, the higher the HbA1C. Since each red blood cell stays in your

circulation for at least three months, the HbA1C level is an accurate reflection of your average blood glucose level over that period of time. Early on HbA1c levels are usually high but then fall to normal levels with effective treatment.

Could I still have diabetes even if I do not have those symptoms?

Yes. The only way to know for sure whether or not you do have diabetes is to go to your doctor and have your blood sugar–glucose-level measured. Blood glucose values are abnormal and indicative of diabetes mellitus when you have:

a. After Overnight Fasting-140 mg/dl on at least two occasions

b. More than 200 mg/dl after a glucose tolerance test

c. Hemoglobin A1C (HbA1C) over 6.5%

Why do I need any treatment? I don't feel sick now. If I just cut out sweets will my diabetes go away?

Diet helps and indeed is the cornerstone for all successful diabetes treatment, but a resolution to cut out hot fudge sundaes and candy bars is not enough. A properly balanced diet that involves three meals a day designed to provide a sensible allotment of protein, fats and carbohydrates is crucial. Your doctor may have a diet plan or he may refer you to a dietician to help tailor a diet just for you. Fad diets are usually not effective and often very dangerous.

But I love to eat. Are there pills to help me control my appetite?

No.Pills that are purported to control appetite like amphetamines rarely work as a long term solution and also worsen diabetes. You can stay on a diet that is tasty and sensible and will help control your diabetes. Once you do you will feel great because you will know that you are able to be in control. Many of my patients do very well with diet alone. Others have to take supplements like insulin or pills in addition to diet to achieve maximal control over their diabetes.

Will I have to give myself insulin injections to manage my diabetes?

It depends on the severity of the diabetes and the insulin deficit. When a person's pancreas stops making insulin completely as is often the case when children or teenagers develop diabetes then insulin injections are necessary. Often a combination of different types of insulin, some with a rapid onset of action and others with more prolonged and sustained blood sugar lowering capacity are needed to bring blood glucose levels down to normal. Work with your doctor, or if he is not familiar with the latest developments in this are ask for a referral to - an endocrinologist - someone who has received special training in the management of patients with diabetes

Who can use pills to treat diabetes?

When diabetes develops later in life the pancreas seems to make some, but not enough insulin. In that instance pills that encourage additional insulin output from the sluggish pancreas help raise the blood insulin level and allow the body to bring blood glucose levels closer to normal. Still other pills improve the efficiency of insulin's actions (insulin sensitizers). When the insulin that your pancreas releases is not as effective as it once was because your body has become resistant to insulin, another generation of pills are specifically designed to overcome your body's insulin resistance. Often a combination of pills is required to first stimulate your pancreas to release additional insulin, then insulin sensitizers to make sure your body responds well to the additional insulin and

finally others to overcome the bodies insulin resistance to maximize the effectiveness of whatever additional insulin is now in your blood stream.

Are there side effects to the pills used to treat diabetes. that they cause liver damage. Can that be true?

All pills even aspirin and other over the counter medications can cause side effects. Side effects seen with treatments for diabetes include:

a. Low blood sugar-hypoglycemia-can occur with pills or insulin.

b. Liver damage-has occurred with troglitazone (Rezulin), and insulin sensitizer that is no longer on the market and rarely with rosiglitazone but not as yet with pioglitazone. Your doctor will do blood tests to check whether your liver has been damaged.

c. Lactic acidosis a rare complication of metformin (Glyciphage) therapy.

Side effects, when they occur are usually reversible with proper treatment.

Living with diabetes can be a challenge, but it doesn't have to stop you from enjoying life.

Do what you can to control your diabetes, follow your doctors advice and you'll find you are living healthier and feeling better than you did before.

Dealing with Infections

Dr. Amrita Misri
Medical Officer
Department of Obstetrics and Gynaecology

Infections that occur within hospitals are the responsibility of the concerned hospital. It is also interesting to note that hospital acquired infections constitute 10 per cent of all hospital admissions worldwide. With the rising number of new and more resistant infective agents being identified, it is the responsibility of each and every individual working in the hospital to comply with the infection control guidelines / policies. Here I am going to mention about the required practices in operation theatre.

Broadly, the practices for operation theatre infection control need to ensure that:

1. Airborne bacteria are minimized.
2. Recommended schedule for cleaning and disinfection of the operation theatre is followed.

I. Airborne contamination is usually affected by the following factors:

- Type of surgery.
- Quality of air provided.
- Rate of air exchange.
- Number of persons present in Operation Theatre.
- Movement of Operation Theatre personnel.
- Level of compliance with infection control.
- Quality of staff clothing.
- Regular cleaning/ servicing of A/C filters.
- Positive air pressure in high risk areas.
- Negative air pressure in contaminated areas.
- AHU / HEPA filters.
- Uni-directional laminar airflow.
- Minimum 15 air changes per hour.
- Temperature: 20-22 deg C; Humidity: 30-60 per cent.
- Supply of adequately sterilized instruments and dressings.
- The handling of biomedical waste till final disposal.

II. Recommended schedule for cleaning and disinfection of the operation theatre.

General Instructions –

- Keep the floor dry when in use.
- Use only vacuum cleaners for cleaning the floors, walls and ceilings.

At the beginning of the day

- Remove dust with cloth wetted with clean water. Clean theatre furniture, lamps, stools, trolley tops, operation tables, procedure tables, anesthesia apparatus etc.

Between the procedures:

- Clean operation tables and contaminated surfaces with disinfectant solutions

- Do not accumulate waste around the operating area.

- Do not discard soiled linen and gowns on the floor in operation theatre.

At the end of the day (after the surgeries)

Through cleaning of all the equipment and floors in operation theatres followed by carbolisation will greatly enhance the safety standards. This requires the trained personnel along with their adequate number. Additionally simple repeated hygienic hand wash is the most cost effective method to reduce several infections in hospitals, in particular operation theatres.

The microbiologist plays the major role in surveillance of operation theatre infections. As bacterial counts in operation theatres are influenced by the number of individuals present, ventilation and air flow, the results should be interpreted taking the above facts into consideration. Microbiologists should choose surveillance cultures carefully to allow meaningful interpretation of results.

To summarize, Operation Theatre discipline involves following guidelines –

1. Only people absolutely needed for an assigned work should be present.

2. People present in theatre should make minimal movements and curtail unnecessary movements in and out of theatres, which will greatly reduce bacterial count.

3. Air borne contamination is usually affected by type of surgery, quality of air which in fact depends on rate of air exchange. All the persons including the least cadre of employees are partners in infection control and should be aware to comply with infection control regulations

4. Prompt disposal of Theatre waste out of the theatre is of top priority. Any spillage of body fluids including blood on the floors is highly hazardous and results in rapid multiplication of nosocomial pathogens in particular Pseudomonas.

So prompt cleaning of any spillage is absolutely necessary.

Ref. WHO guidelines for Infection Control

Hand washing & Decontamination

Hand washing is the most effective method of preventing the transfer of bacteria between health care provider and the patient.

Presentations / Achievements / Seminars

Department: Obstetrics & Gynaecology Scientific Paper Presentations

1. Title: "Ideal use of CTG in decision making for LSCS." Authors: Dr. Nigamanand Mishra, Dr. Amrita Misri and Dr. D.P. Joshi. Presentation by: Dr. Nigamananda Mishra, Medical officer.Venue: All India Conference in Obstetrics & Gynaecology 2009, Jaipur. Date: 8th January 2009.

2. Title: "Effect of amino acid supplementation on birth weight."Authors: Dr. B. Rao Bahadur, Dr. Bhushan Patil and Dr. Amrita Misri.Presentation by: Dr. B. Rao Bahadur, Resident Medical officer.Venue: All India Conference in Obstetrics & Gynaecology 2009, Jaipur.
   Date: 8th January 2009.

3. Title: Surgeon's Signature: Suture Vs Stapler. Authors: Dr. Veena Acharya, Dr. Amrita Misri and Dr. Santoshi Prabhu.Presentation by: Dr. Veena Acharya, Resident Medical officer. Venue: 37th Annual Conference of Mumbai Obstetrics & Gynaecological society at LTM College, Sion Hospital, Mumbai.
   Date: 6th March 2009.

4. Title: "Closure Matters: Effect of peritoneal closure at Caesarean section on adhesion formation in future."Authors: Dr. Santoshi Prabhu, Dr. Amrita Misri and Dr. D.P. Joshi. Presentation by: Dr. Santoshi Prabhu, Medical officer. Venue: 37th Annual Conference of Mumbai Obstetrics & Gynaecological society at LTM College, Sion Hospital, Mumbai.
   Date: 6th March 2009.

Dr. Santoshi Prabhu received 'Dr. N.A. Purandare Prize' for Operative Obstetrics- Senior category.

Department: Trombay Dispensary Scientific Paper Presentations

1. Title: "Studies on the immunological basis of allergic disorders" Authors: Dr. V. Kohli, Dr. K.B. Sainis Presented by: Dr. Vineet Kohli Conference: Annual Bio-medical Research Test Venue: Training School Hostel, Anushaktinagar, Mumbai
   Date: 25th March 2009

2. Title: Allergy prevalence and risk factors in Mumbai and immune response in allergic subjects Authors: Dr. V. Kohli, Dr. D. Sharma, Dr. S. Sandur, Dr. K.B. Sainis
   Presented by: Dr. Vineet Kohli Conference: 7th European Academy of Allergy and Clinical Immunology (EAACI)-GA2LEN Immunology winter school meeting Venue: Sunstar Park Hotel Davos, Switzerland
   Date: 5th – 8th February 2009

Department: Pathology Poster Presentation

Title: "Comparison in Infectious Disease Mark ers in Voluntary & Replacement Donors"
Authors: Dr. Veena Arora, Dr. R.K. Kulkarni
Presented by: Dr. Veena Arora, Medical officer
Venue: 33rd National Conference of Indian society of Blood Transfusion & Immunohaematology, TRANSCON 2008, at Sanjay Gandhi Post Graduate Institute of Medical Science Lucknow
Date: 5th - 7th December 2008.

Seminars organized

Atomic Energy Education Society in collaboration with doctors from BARC Hospital had organized a Health Awareness Seminar at M.P. Hall, Training School Hostel, Anushaktinagar on 8th November, 2008. Seminar was conducted in two sessions chaired by Dr. J.K. Jaitley and Dr. P.K. Sinha. Following topics were covered:

- Health and nutrition – Dr. Rekha Bhatkhande
- Yoga for better health- Dr. Asha Damodaran
- Ageing gracefully- Dr. A.R. Kulkarni
- Garbage management and health- Dr. S.P. Kale
- Life style related diseases- Dr. Anuradha Chakraborty

Hindi Vigyan Sahitya Parishad BARC, headed by Dr. K.B. Sainis had organized a seminar as a part of Manav Swasth Sangosthi Srinkhala, for the CHSS beneficiaries. On Management of infertility and adoption, its social and legal issues, at AERB Auditorium, on 21st March 2009 . Following topics were covered:

Speaker	Topic
Dr. Amrita Misri	Introduction toinfertility and counseling of infertile couple
Dr. Amit Patki	Infertility diagnosis and management.
Dr. Nikhil Datar	Patients expectations and doctors restrictions in infertility management.
Dr. Nigamananda Mishra	Male infertility.
Prof. Dr. K.B. Argade	Adoption, its social and ethical issues.
Dr. Mrs. Pramila Jarag	Legal issues in adoption

हिंदी विज्ञान साहित्य परिषद विगत कई वर्षो से प्रगत वैज्ञानिक विषयों को राजभाषा हिंदी के माध्यम से जनसामान्य एवं वैज्ञानिक समुदाय तक पहुचाने का कार्य कृत संकल्प भाव से करती आ रही है। अपनी इस प्रतिवध्दता का अनुपालन करते हुए परिषद लगभग हर वर्ष स्वास्थ्य संबंधी विषयों पर संगोष्ठियां आयोजित करती है। ये संगोष्ठियां परमाणु ऊर्जा विभाग के परिवार के सदस्यों में अत्यंत लोकप्रिय है। इस वर्ष परिषद जनन अक्षमता - समस्यायें एवं निदान तथा अंगीकरण - अडाप्शन - के सामाजिक एवं न्यायायिक पहलू विषय पर एक दिवसीय संगोष्ठी आयोजित की थी। इस संगोष्ठी में छह वार्ताएं तथा अंत में प्रतिभागियों के प्रश्नों पर चर्चा हुई। यह संगोष्ठी परमाणु ऊर्जा नियामक परिषद सभागृह, अणुशक्तिनगर में दिनांक २१ मार्च २००९ को आयोजित की गई।

श्री डा. के.बी. सैनिस की अध्यक्षता में, सचिव श्री जयप्रकाश त्रिपाठी और स्त्रीरोग विशेषज्ञ डा. अमृता मिसरी एवं डा. निगमानंद मिश्रा ने इस संगोष्ठी का संयोजन किया।

Medical division Annual Day January 13, 2009

Scientific talk on "Current Perspectives in Women's Health" by an eminent gynaecologist, Dr. Usha Saraiya.

Inauguration of Annual day issue of Pulse by Dr. S. K. Banerjee,Director; BARC.

Medical Guidelines for patient care inaugurated by Dr.K.B.Sainis, Director Biomedical Group .

Dr. V.Karira, Head Medical Division inaugurating booklet on Diabetes.

Audience at Scietific Session

Walkathon January - 2009

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