Diabetes physiology and inpatient Hospital Care

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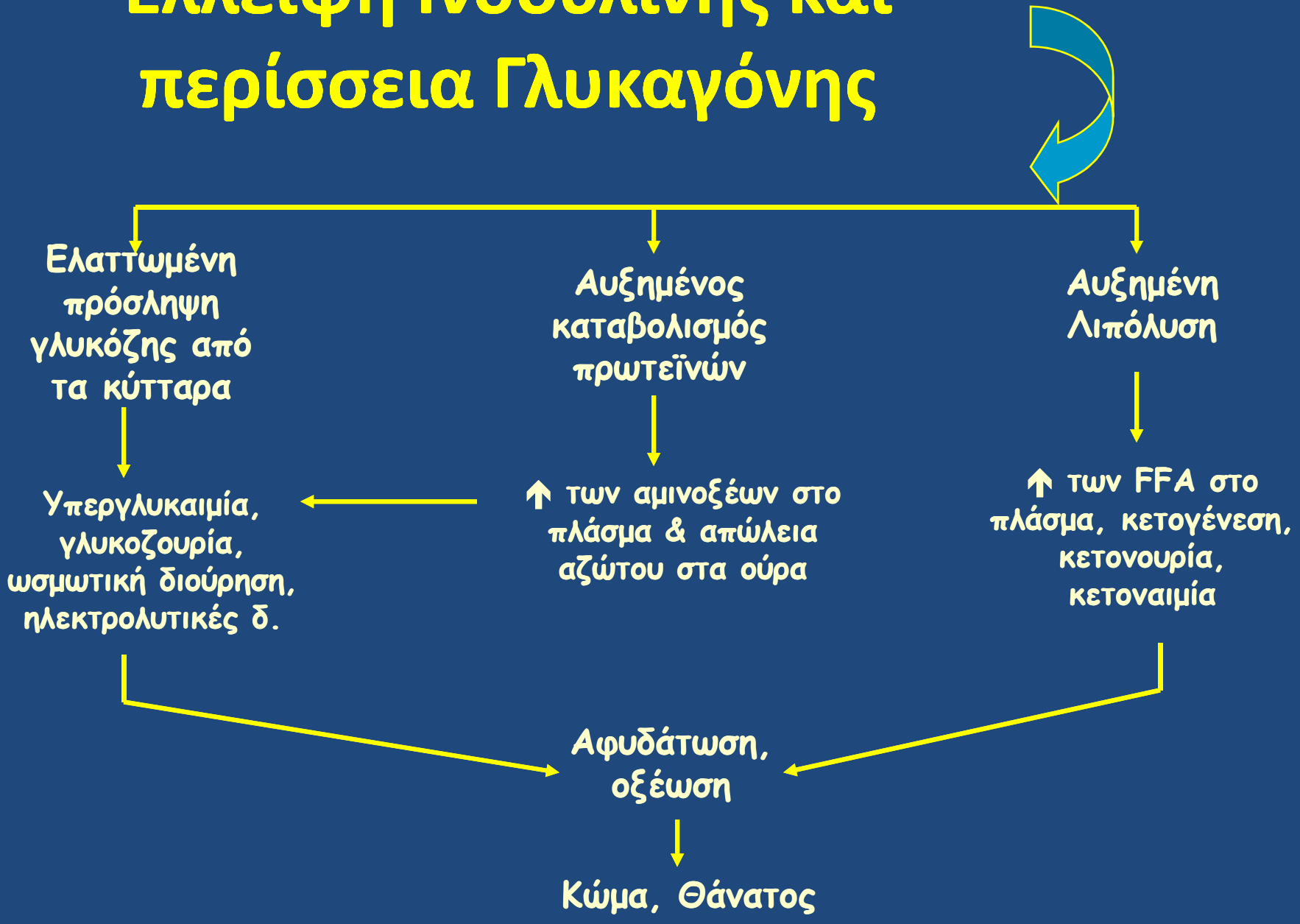
Έλλειψη Ινσουλίνης και περίσσεια Γλυκαγόνης



Κετόνες ή κετονικά σώματα

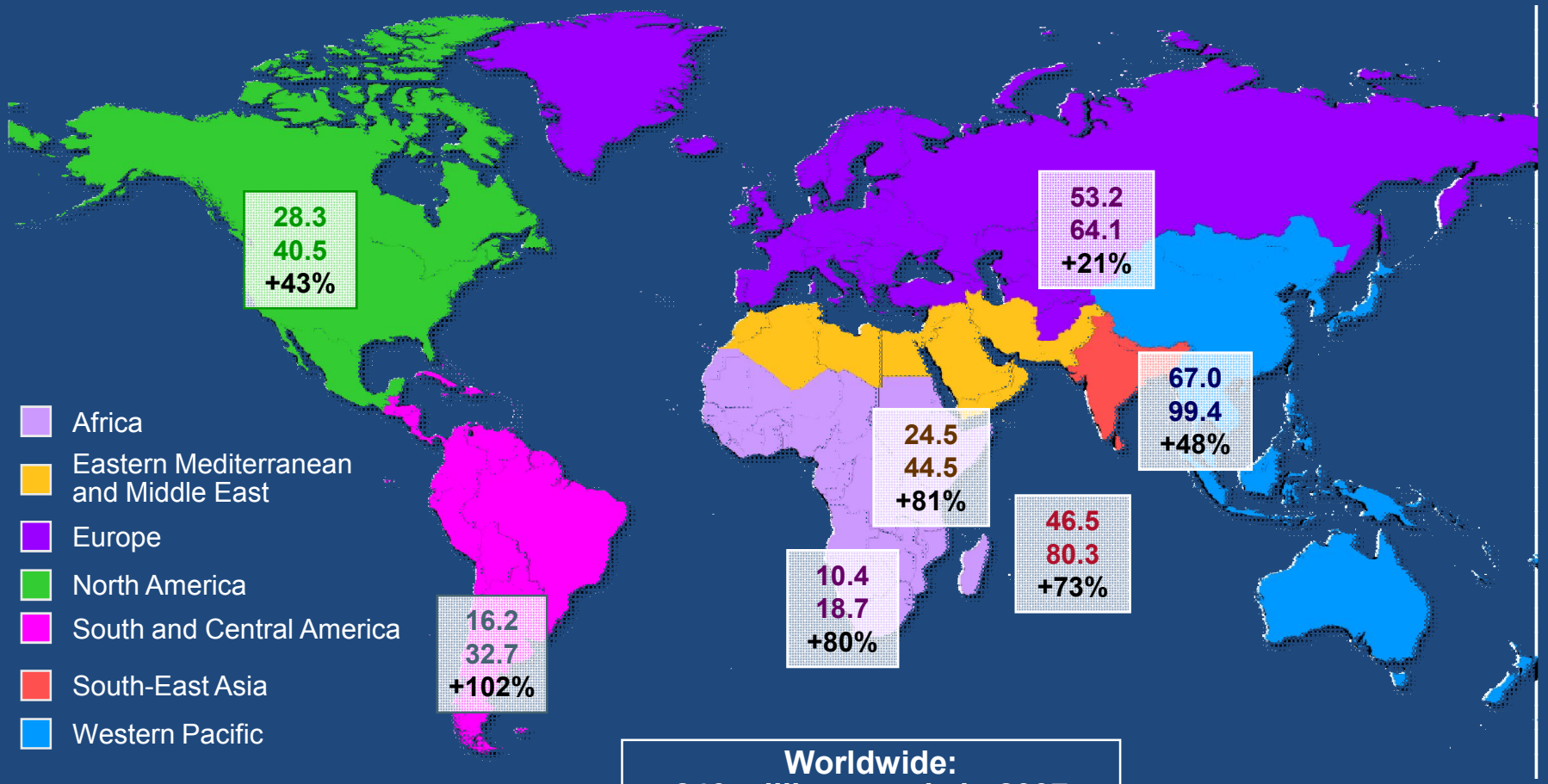
- Ακετόνη, ακετοξεικό & β-υδροξυβουτυρικό
- Είναι πηγή ενέργειας, σημαντική ενίοτε
- Παράγονται φυσιολογικά σε επίπεδα < 1-3mg/dL στο αίμα, κατά τον καταβολισμό των λιπιδίων
- Η ακετόνη αποβάλλεται δια της αναπνοής & των ούρων
- Όταν η ικανότητα των ιστών για τον μεταβολισμό τους σύντομα υπερκεράζεται, οδηγούμεθα σε κέτωση και κετοξέωση (πτώση του pH <7.35)

Η σημασία του μεταβολικού ελέγχου

" Ο *Σ. Διαβήτης* χαρακτηρίζεται από την ανεπάρκεια του συστήματος ελέγχου του μεταβολισμού της γλυκόζης, οδηγώντας σε χρόνια αύξηση των επιπέδων γλυκόζης αίματος"

Diabetes is an increasing healthcare epidemic throughout the world

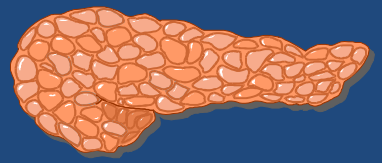
Global projections for the number of people with diabetes
(20–79 age group), 2007–2025 (millions)



Worldwide:
246 million people in 2007
380 million projected for 2025

IDF. Diabetes Atlas 3rd Edition – 2006

Εισαγωγή



Το έργο της ινσουλίνης είναι :

- ✓ Η ανταπόκριση στις μεταβολές των επιπέδων γλυκόζης αίματος
- ✓ Η διατήρηση των επιπέδων γλυκόζης εντός φ.ο. – σχετικά στενών *(70-110 mg/dL ή 3-6 mmol/L)*
- ✓ Η μακροχρόνια διατήρηση του γλυκαιμικού ελέγχου

Η παραγωγή και απελευθέρωση της ινσουλίνης

- Η ινσουλίνη είναι μια ορμόνη που παράγεται από τα ***β - κύτταρα*** του παγκρέατος με την μορφή πρόδρομου μορίου, της ***προϊνσουλίνης***

- Η προϊνσουλίνη στη συνέχεια ***αποδομείται*** προς ινσουλίνη και ένα μικρότερο μόριο, που ονομάζεται ***C-πεπτίδιο***

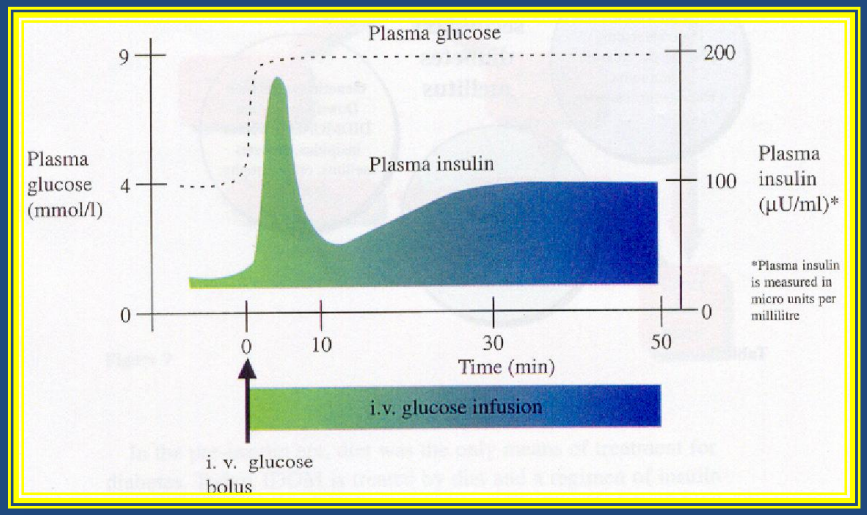
- Στη συνέχεια και τα δυο, ινσουλίνη και C- πεπτίδιο, ***αποθηκεύονται*** εντός κοκκίων που βρίσκονται στα β - κύτταρα του παγκρέατος

- Τα ***βασικά επίπεδα*** ινσουλίνης που απαιτούνται για τη διατήρηση των φυσιολογικών επιπέδων γλυκόζης (ευγλυκαιμία), αναλογούν περίπου στο ***ήμισυ της συνολικής*** ποσότητας ινσουλίνης που εκκρίνεται σε μια περίοδο 24 ωρών

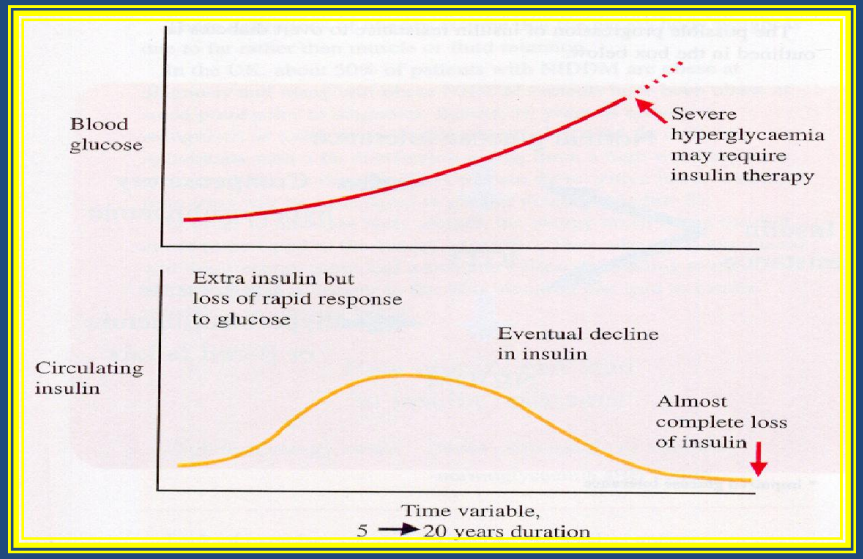
- Η υπόλοιπη ποσότητα παραγόμενης ινσουλίνης προορίζεται για την ανταπόκριση του οργανισμού ***στις μεταγευματικές αυξήσεις*** των επιπέδων γλυκόζης αίματος (δηλαδή μετά την πρόσληψη τροφής)

Η παραγωγή και απελευθέρωση της ινσουλίνης στον ΣΔ τ. 2

✓ Στα μη Διαβητικά άτομα η έκκριση-απελευθέρωση ινσουλίνης λαμβάνει χώρα σε 2 φάσεις : μια πρώτη ταχεία και βραχυχρόνια & μια δεύτερη φάση, πιο βραδείας ανόδου αλλά πιο παρατεταμένη



✓ Στα Διαβητικά άτομα τ.2 η πρώτη ταχεία και βραχυχρόνια φάση έχει απωλεσθεί & έτσι δεν υφίσταται ταχεία ανταπόκριση στην αύξηση της γλυκόζης. Η δεύτερη φάση, στα πρώϊμα στάδια του ΣΔ τ.2 είναι αυξημένη, σε ανταπόκριση της απώλειας της 1ης φάσης, αλλά γίνεται σταδιακά μικρότερη καθώς προχωρά η έκπτωση των β-κυττάρων, με αποτέλεσμα υπεργλυκαιμία



2013 Recommendations

ADA Guidelines: Criteria for Diabetes Diagnosis

A1C ≥6.5%*†

OR

FPG‡ ≥126 mg/dL (7.0 mmol/L)†

OR

2-hr plasma glucose ≥200 mg/dL (11.1 mmol/L) during OGTT (75-g)†

OR

Random plasma glucose ≥200 mg/dL (11.1 mmol/L)**

*Perform in lab using NGSP-certified method and standardized to DCCT assay; †In the absence of unequivocal hyperglycemia, result to be confirmed by repeat testing; ‡Fasting defined as no caloric intake for ≥8 hrs; **in persons with symptoms of hyperglycemia or hyperglycemic crisis

American Diabetes Association. *Diabetes Care*. 2013;36(suppl 1):S11-S66.

2013 Recommendations

ADA Guidelines: Common Comorbidities Associated With Diabetes

Consider assessment and treatment for common diabetes-associated comorbidities in patients with risk factors, signs, or symptoms of

- Certain cancers
- Cognitive impairment
- Depression
- Dyslipidemia
- Fatty liver disease
- Fractures
- Hearing impairment
- Hypertension
- Low testosterone (men)
- Obesity
- Obstructive sleep apnea
- Periodontal disease

American Diabetes Association. *Diabetes Care*. 2013;36(suppl 1):S11-S66.

2013 Recommendations

ADA Guidelines: Criteria for Diabetes Testing in Asymptomatic Adults

- Consider testing for diabetes in all adults with BMI* ≥25 kg/m^2 and ≥1 additional risk factor
  - In the absence of risk factors, testing should begin no later than age 45
- If results are normal, repeat testing in ≥3-year intervals
  - More frequent testing may be done depending on initial test results and presence of risk factors

Diabetes Risk Factors

- Physical inactivity
- First-degree relative with diabetes
- High-risk race/ethnicity
- Women who delivered a baby >9 lb or were diagnosed with GDM
- HDL-C <35 mg/dL and/or TG >250 mg/dL
- Hypertension (≥140/90 mm Hg or on therapy)
- A1C ≥5.7%, IGT, or IFG on previous testing
- Conditions associated with insulin resistance: severe obesity, acanthosis nigricans, PCOS
- History of cardiovascular disease

*At-risk BMI may be lower in some ethnic groups

BMI=body mass index; GDM=gestational diabetes mellitus; HDL-C=high-density lipoprotein cholesterol; IFG=impaired fasting glucose; IGT=impaired glucose tolerance; PCOS=polycystic ovarian syndrome; TG=triglycerides

American Diabetes Association. *Diabetes Care*. 2013;36(suppl 1):S11-S66.

2013 Recommendations

ADA Guidelines: Categories of Increased Risk for Diabetes (Prediabetes)

FPG 100 mg/dL–125 mg/dL (5.6 mmol/L–6.9 mmol/L)
Impaired Fasting Glucose

OR

2-hr PG on 75-g OGTT 140 mg/dL–199 mg/dL
(7.8 mmol/L–11.0 mmol/L)
Impaired Glucose Tolerance

OR

A1C 5.7%–6.4%

- For all tests, risk is continuous, extending below lower limit of range and becoming disproportionately greater at higher ends of range
- IFG and IGT should be viewed as risk factors for diabetes and CVD

CVD=cardiovascular disease; FPG=fasting plasma glucose; OGTT=oral glucose tolerance test; PG=plasma glucose

American Diabetes Association. *Diabetes Care*. 2013;36(suppl 1):S11-S66.

2013 Recommendations

ADA Guidelines: Primary Prevention of Type 2 Diabetes With Medical Nutrition Therapy

Individuals at high risk for developing type 2 diabetes:

- Begin a structured program emphasizing lifestyle changes, including:
  - Moderate weight loss (7% body weight)
  - Regular physical activity (150 min/wk) with dietary strategies, incl reduced calories and dietary fat intake
- Achieve USDA recommendation for dietary fiber (14 g/1,000 kcal) and foods containing whole grains (50% of grain intake)
- Limit intake of sugar-sweetened beverages

USDA=U.S. Department of Agriculture

American Diabetes Association. *Diabetes Care*. 2013;36(suppl 1):S11-S66.

ADA Guidelines: Diabetes Care in the Hospital (1 of 2)

- Clearly document diabetes in medical record
- Order blood glucose monitoring for all patients
  - Results available to healthcare team
- Goals for blood glucose levels in critically ill patients
  - Initiate insulin for treatment of persistent hyperglycemia starting at threshold of ≤180 mg/dL (10.0 mmol/L); once insulin is started, 140–180 mg/dL (7.8–10.0 mmol/L) is recommended range for most patients
  - More stringent goals may be appropriate for certain patients
  - IV insulin protocol with demonstrated efficacy, safety in achieving glucose targets with no increased hypoglycemia risk
- Goals for blood glucose in non–critically ill patients
  - No clear evidence for specific goals
  - Insulin-treated: premeal target <140 mg/dL (7.8 mmol/L) with random blood glucose <180 mg/dL (10.0 mmol/L)
  - More or less stringent targets may be appropriate for certain patients

Continued on next slide

American Diabetes Association. *Diabetes Care*. 2013;36(suppl 1):S11-S66.

ADA Guidelines: Diabetes Care in the Hospital (2 of 2)

- Preferred method for achieving/maintaining glucose control in non–critically ill patients
  - Scheduled subcutaneous insulin with basal, nutritional, and correction components
- Monitor glucose in nondiabetic patients receiving therapy associated with high risk for hyperglycemia
  - Consider treating to same goals as patients with known diabetes
- Establish hypoglycemia management protocol and create a plan for each patient for treating and preventing hypoglycemia
  - Track all hypoglycemia episodes
- Consider obtaining A1C for
  - Patients with diabetes if no previous test results from last 2–3 mos available
  - Patients with risk factors for undiagnosed diabetes who exhibit hyperglycemia
- Patients with hyperglycemia with no prior diabetes
  - Plan for follow-up testing and care documented at discharge

American Diabetes Association. *Diabetes Care*. 2013;36(suppl 1):S11-S66.

Hospital System Enhancements for Safe Insulin Use

- Standardized protocols promote the safe use of insulin in hospitals
- Complicated insulin regimens can lead to confusion and medication errors,
- it is recommended to simplify insulin regimens as much as possible.

Hospital System Enhancements for Safe Insulin Use

- Simplification of the hospital insulin formulary is the first step, limiting clinicians to a single basal insulin and a single rapid-acting insulin choice.
- Monitoring and documentation of insulin administration and glucose measurement should be together as a single document (either paper flow sheet or a single EMR screen).

- a stepped implementation of SC insulin protocols (paper-based or via electronic medical record [EMR]) leading to mandatory use of basal/bolus insulin on a hospital-wide basis is optimal.

Hospital Blood sugar controls

- from 31 U.S. hospitals. more than 1.5 million blood sugars
- showed an average per patient-day mean glucose of 151.8 mg/dL in ICU patients and 152.7 mg/dL in non-ICU patients.
- Outside the ICU, a mean target glucose of 70–149 mg/dL was achieved in 55.8% of the patients, and 9.5% of patient-days had at least 1 hypoglycemic episode

Data derived from surgical and medical intensive care units

- Observational studies have documented that hyperglycemia after cardiothoracic surgical procedures is associated with higher rates (approximately twofold) of wound infection
- Interventions to reduce hyperglycemia in this setting with IV insulin therapy decrease infection rates and cardiac-related mortality in comparison with historical control subjects.

critically ill patients in medical and surgical intensive care units (ICUs)

- Intensive insulin therapy targeting arterial glucose levels of 80–110 mg/dl in 1,200 medical ICU patients by the same investigators in the same institution diminished morbidity but failed to reduce mortality (θνησιμοτητα).

critically ill patients in medical and surgical intensive care units (ICUs)

- A sixfold increase in severe hypoglycemic events (BG <40 mg/dl [2.2 mmol/l]) was observed in the intensively treated group (18.7 vs. 3.1%),

- hypoglycemia was identified as an independent risk factor for mortality

critically ill patients in medical and surgical intensive care units (ICUs

- (NICE-SUGAR), a multicenter, multinational RCT,
- tested the effect of tight glycemic control on outcomes among 6,104 critically ill participants, the majority of whom (>95%) required mechanical ventilation.

critically ill patients in medical and surgical intensive care units (ICUs)

- The 90-day mortality was significantly higher in the intensively treated versus the conventionally treated group (78 more deaths; 27.5 vs. 24.9%; P = 0.02) in both surgical and medical patients

critically ill patients in medical and surgical intensive care units (ICUs)

- Mortality from cardiovascular causes was more common in the intensively treated group (76 more deaths; 41.6 vs. 35.8%; $P = 0.02$). Severe hypoglycemia was also more common in the intensively treated group (6.8 vs. 0.5%; $P < 0.001$).

critically ill patients in medical and surgical intensive care units (ICUs)

- A recent meta-analysis of RCTs reported comparisons between intensive insulin therapy with glycemic targets of 80 to 110 mg/dl and less intensive therapy with targets 180 to 200 mg/dl [10.0–11.1 mmol/l]).

critically ill patients in medical and surgical intensive care units (ICUs)

- Among 8,432 critically ill patients, there was no significant difference in mortality between intensive therapy and control groups (21.6 vs. 23.3%, respectively)
- A decrease in septicemia and a fivefold increase in hypoglycemia (13.7 vs. 2.5%) were observed

critically ill patients in medical and surgical intensive care units (ICUs)

- In a second meta-analysis including 13,567 critically ill patients,
- a favorable effect of intensive therapy on mortality was noted only in surgical ICU patients (relative risk, 0.63; CI, 0.44 to 0.91)
- There was a sixfold increase in the rate of occurrence of hypoglycemia with use of intensive therapy in all ICU patients

critically ill patients in medical and surgical intensive care units (ICUs)

- Hypoglycemic events, however, have been infrequently linked to mortality; this finding suggests that severe hypoglycemia may be a marker of more serious underlying disease

Data derived from patients with acute myocardial infarction

- hyperglycemia is associated with adverse outcomes after acute myocardial infarction
- reduction of glycemia per se, and not necessarily the use of insulin, is associated with improved outcomes

Data derived from patients with acute myocardial infarction

- It remains unclear, whether hyperglycemia is a marker of underlying health status or is a mediator of complications after AMI
- Non-iatrogenic hypoglycemia has also been associated with adverse outcomes and is a predictor of higher mortality

Data derived from patients with acute myocardial infarction

- Several studies have attempted to reproduce the favorable outcomes observed with early implementation of insulin therapy reported in the first Diabetes and Insulin-Glucose Infusion in Acute Myocardial Infarction (DIGAMI) trial
- DIGAMI 2, a multicenter RCT of 1,253 patients with AMI and diabetes, failed to show a decrease in mortality with such intervention

Data derived from other critically ill patients

- glycemia and clinical outcomes in patients with extensive burns, body trauma, or traumatic brain injury or who have undergone surgical treatment for cerebral aneurysms
- In patients with subarachnoid hemorrhage, hyperglycemia was associated with impaired cognition and deficits in gross neurologic function at 3 months

Data derived from other critically ill patients

- Patients without diabetes who had severe blunt injury and hyperglycemia (BG >200 mg/dl) were found to have a 2.2-fold higher rate of mortality than those with admission glucose of <200 mg/dl

Data derived from other critically ill patients

- In an RCT of tight glycemic control in 97 patients with severe traumatic brain injury no significant differences were noted in infections, 6-month mortality, or neurologic outcomes. The rate of occurrence of hypoglycemia was twofold higher with use of intensive insulin therapy.

Data derived from patients undergoing transplantation

- Diabetes in patients after transplant procedures shares many similarities with type 2 diabetes and is strongly associated with cardiovascular disease and cardiac death

Data derived from patients undergoing transplantation

- Hammer et al. analyzed BG levels among 1,175 adult patients receiving allogeneic hematopoietic cell transplants.
- Hyperglycemia, hypoglycemia, and glycemic variability all correlated with non–relapse-related mortality within 200 days after transplantation

Hyperglycemia in hospitalized medical and surgical patients in non-ICU settings

- No RCTs have examined the effect of intensive glycemic control on outcomes in hospitalized patients outside ICU settings

Hyperglycemia in hospitalized medical and surgical patients in non-ICU settings

- Several observational studies, however, point to a strong association between hyperglycemia and poor clinical outcomes, including prolonged hospital stay, infection, disability after discharge from the hospital, and death