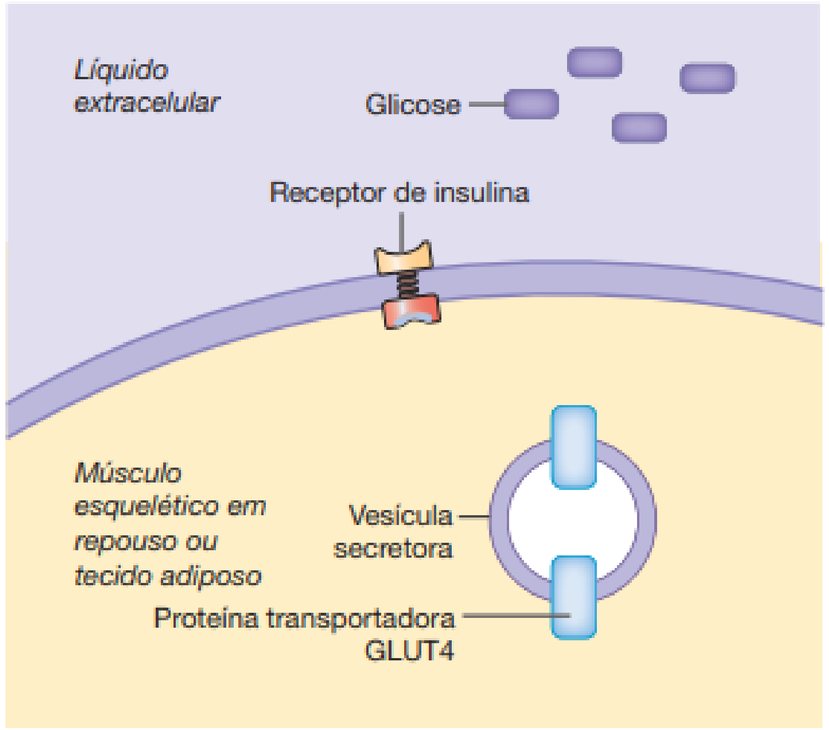
BASES ENDÓCRINAS DA DIABETES MELLITUS

Metabolismo do indivíduo sadio

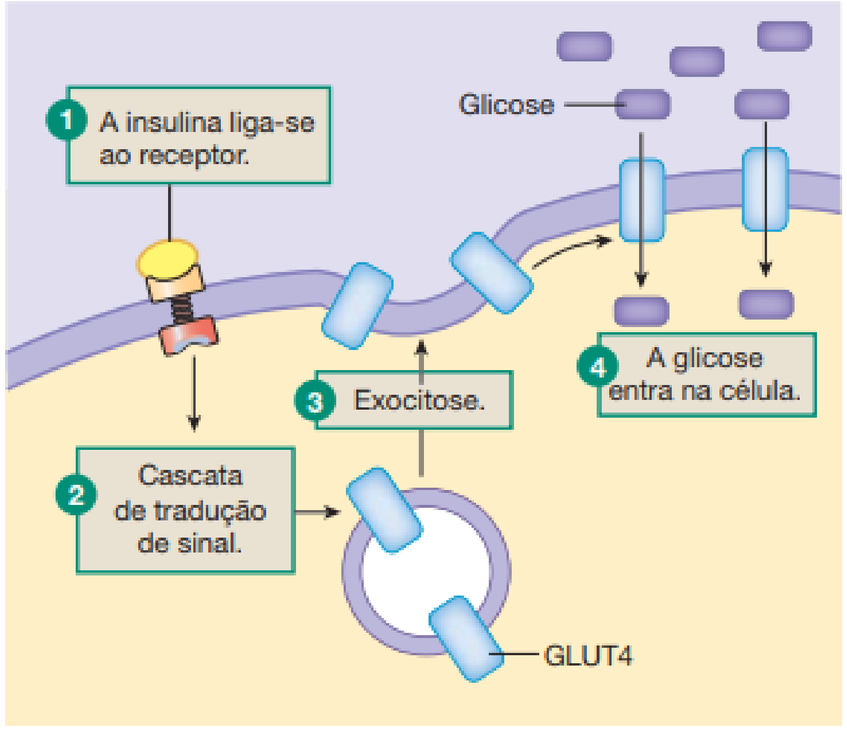
ESTADO DE JEJUM	ESTADO ALIMENTADO

Tecido adiposo e músculo esquelético em repouso

(a) Na ausência da insulina, a quantidade de transportatores GLUT4 na membrana da célula fica muito reduzida.

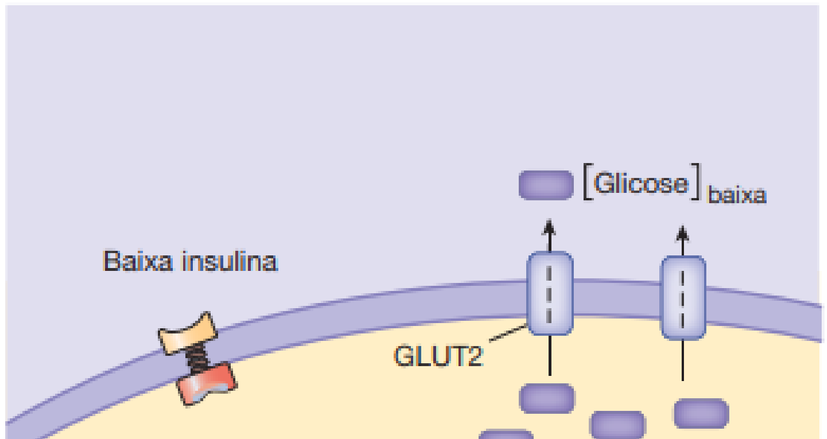


(b) No estado alimentado, a insulina sinaliza para as células a necessidade de produzir e inserir transportadores GLUT4 na membrana, permitindo uma grande antrada de glicose para dentro da célula.

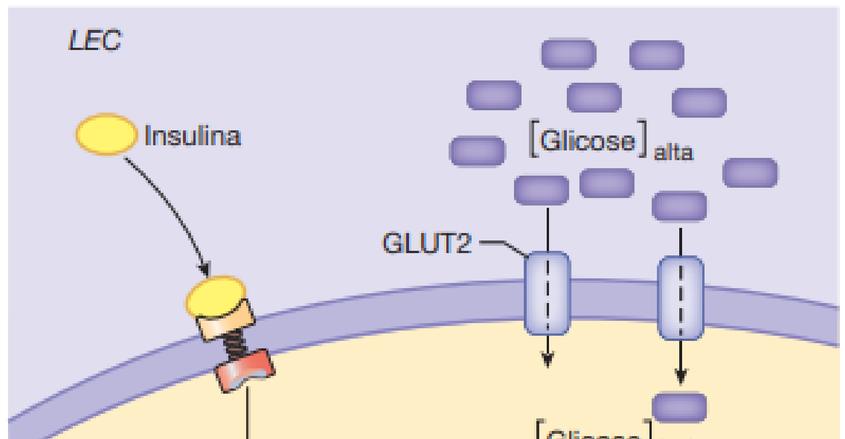


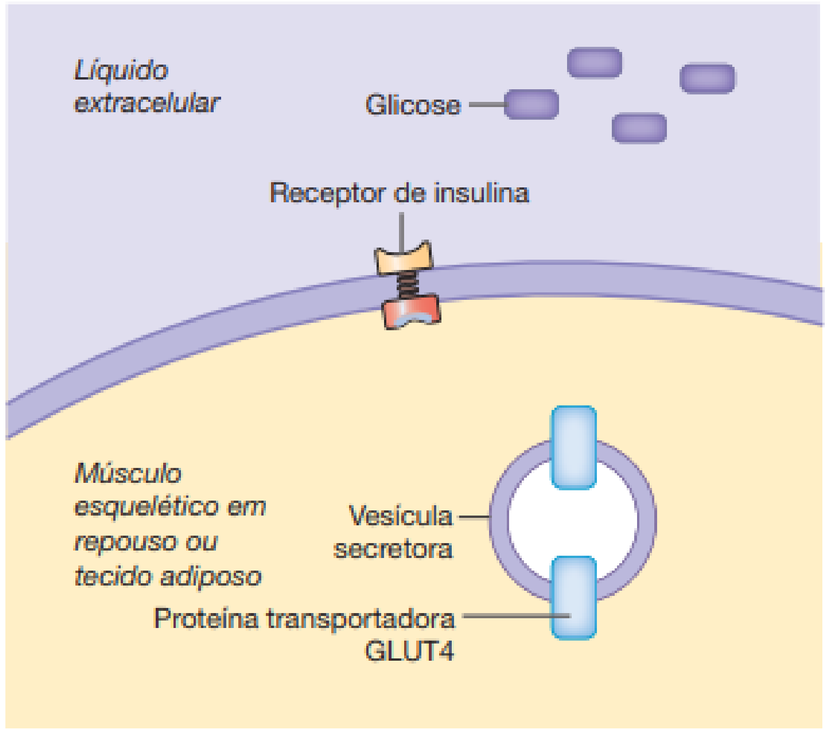
Hepatócitos

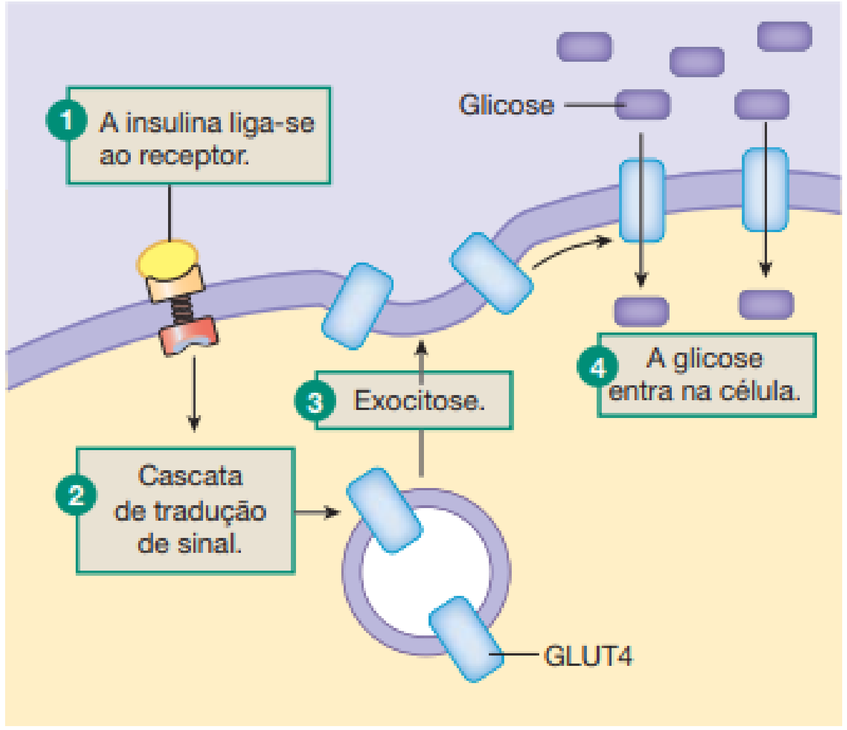
(c) No estado de jejum, os hepatócidos sintetizam glicose e a transportam para o sistema circulatório através de transportadores GLUT2.



(d) No estado alimentado, o gradiente de concentração da glicose reverte-se, e a glicose entra para dentro dos hepatócitos.







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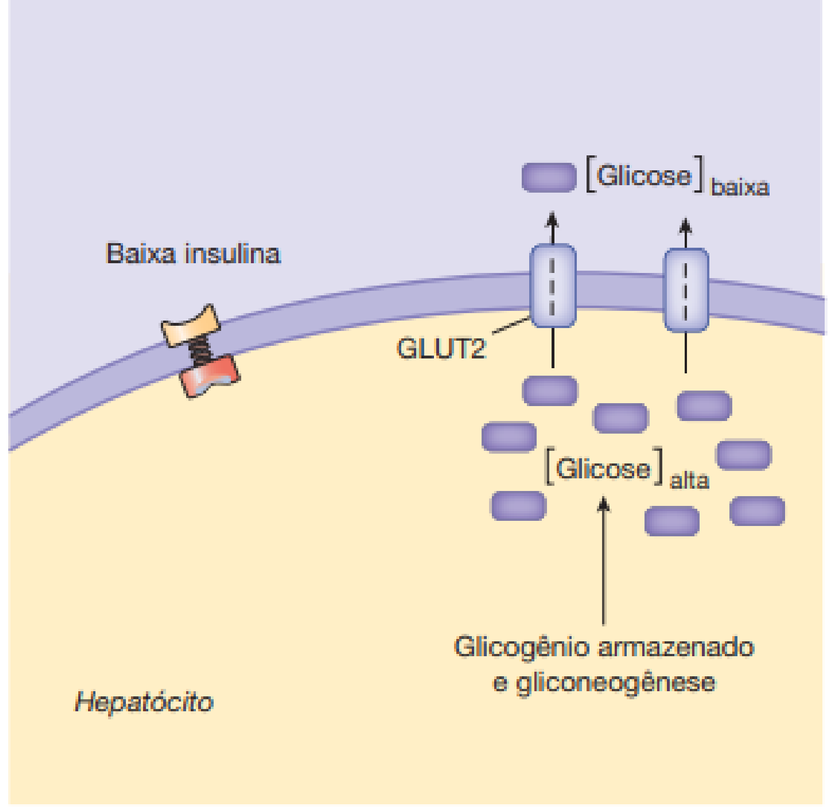

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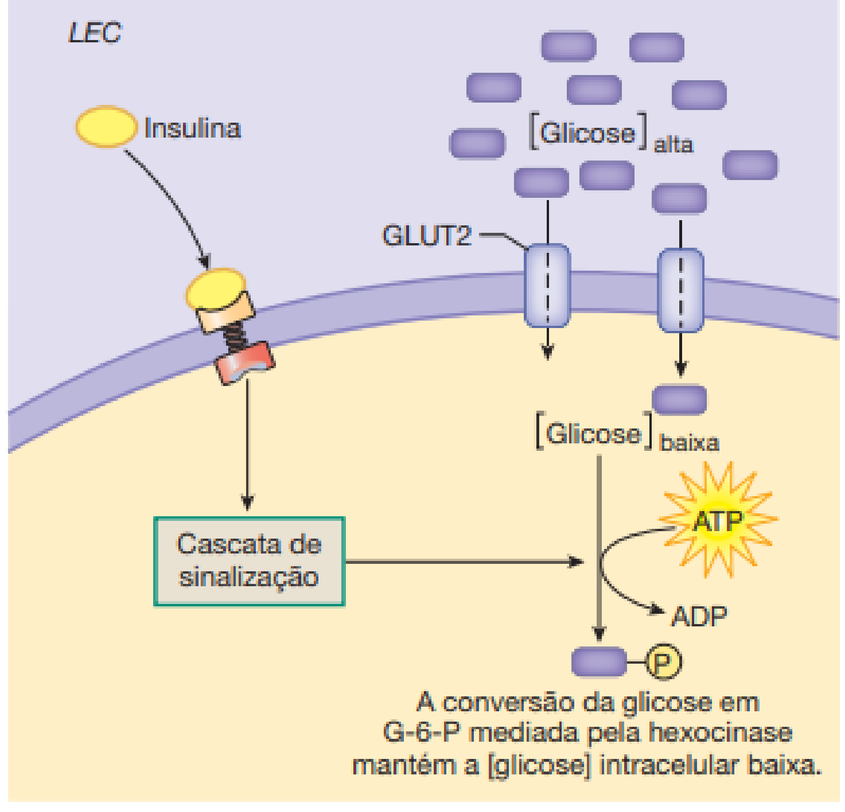
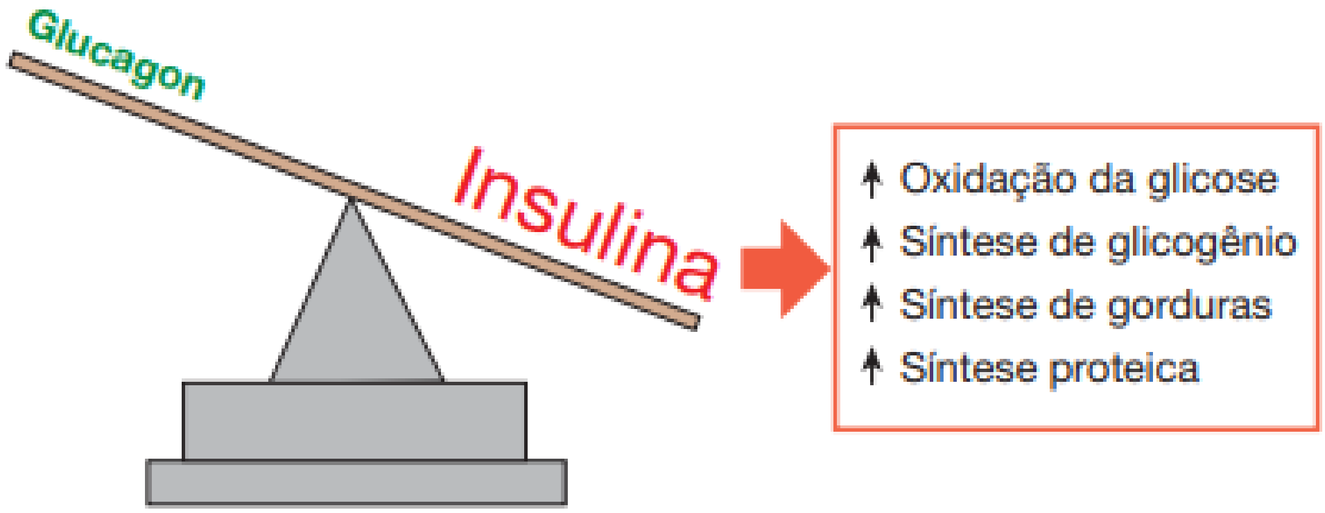
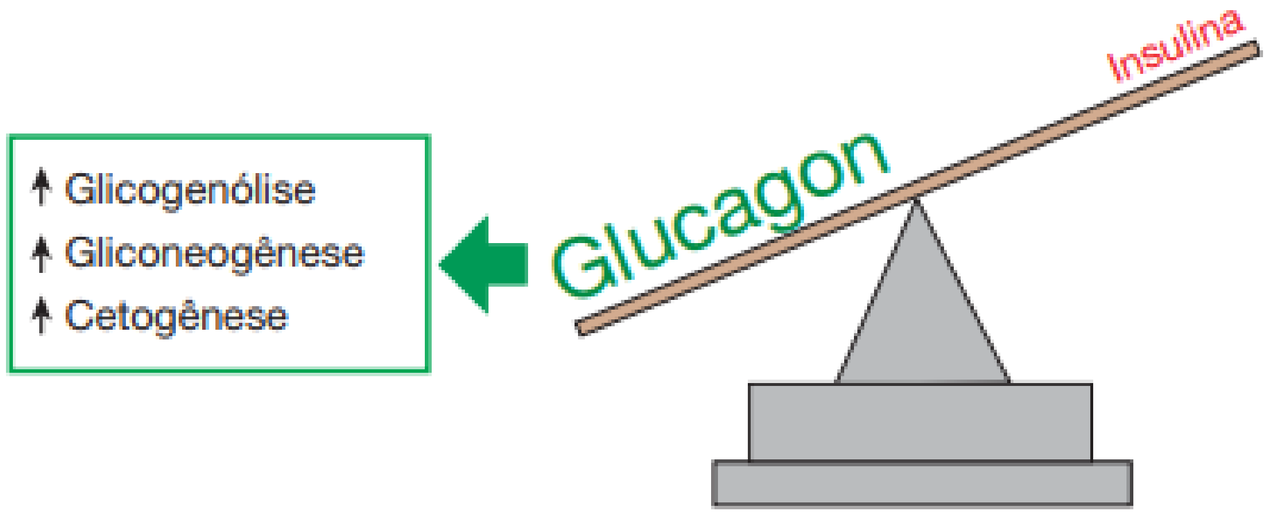


Relação insulina glucagon

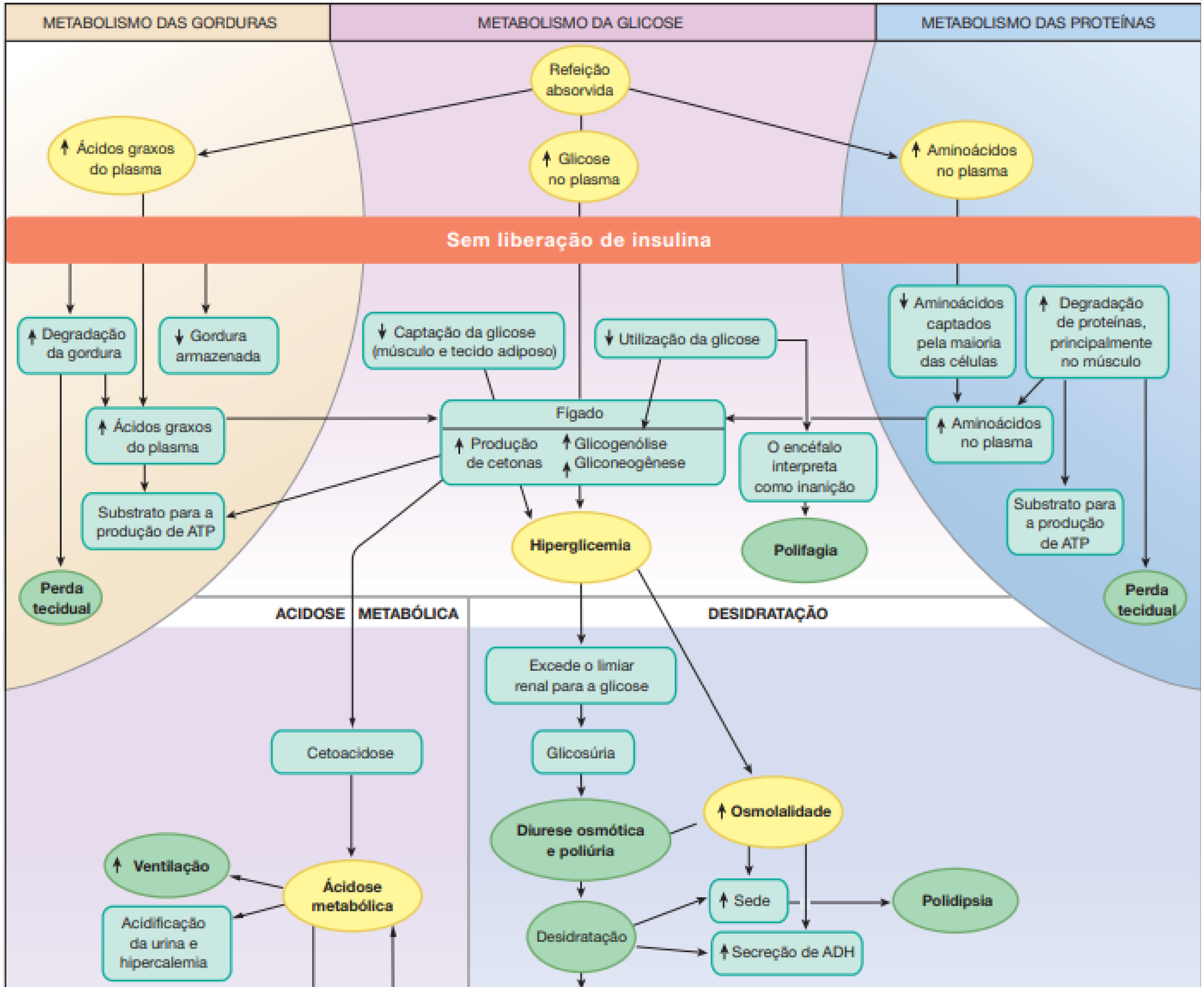
(a) Estado alimenado: domínio da Insulina



(b) Estado de jejum: domínio do glucagon



Metabolismo do diabético tipo 1



↑ Ácidos graxos do plasma

Substrato para a produção de ATP

Perda tecidual

↑ Produção de cetonas

↑ Glicogenólise

↑ Gliconeogênese

O encéfalo interpreta como inanição

Polifagia

↑ Aminoácidos no plasma

Substrato para a produção de ATP

Perda tecidual

Hiperglicemia

ACIDOSE METABÓLICA

DESIDRATAÇÃO

Cetoacidose

↑ Ventilação

Ácidose metabólica

Acidificação da urina e hipercalemia

Produção de ácido láctico

Metabolismo anaeróbio

Excede o limiar renal para a glicose

Glicosúria

Diurese osmótica e poliúria

↑ Osmolalidade

↑ Sede

Polidipsia

Desidratação

↑ Secreção de ADH

↓ Volume sanguíneo e ↓ pressão arterial

Tentativa de compensação pelo centro de controle cardiovascular

Insuficiência circulatória

Se a compensação falhar

Coma ou morte

Diferenças entre Diabetes

Tipo 1	Tipo 2
• Doença autoimune • não há produção de insulina • Células Beta foram destruídas • Dependente de insulina para o resto da vida • Normalmente inícia na juventude, mas pode ocorrer em qualquer idade	• Resistência a insulina • Produz ou não insulina suficiente, mas o corpo é resistente a ela • Células Beta deterioram com o passar do tempo • Prédisposição genética • Normalmente surge por volta dos 45 anos • Obesidade

Sintomas da hiperglicemia

Polidipsia
(sede incessante)

Polifagia
(fome constante)

Poliúria
(vontade de urinar frequente)

Visão turva

Xerostomia
(sensação de boca seca)

Cansaço

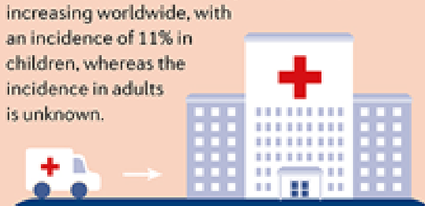
Relação eletrolítica

For the Primer, visit doi: 10.1038/s41572-020-0180-2

Diabetic ketoacidosis (DKA) is the most common hyperglycaemic emergency in people with diabetes mellitus and results in the triad of events of hyperglycaemia, ketosis and metabolic acidosis.

EPIDEMIOLOGY

The incidence of DKA is 13–80% in both adults and children with type 1 diabetes mellitus (T1DM). The incidence of DKA as the initial presentation of T2DM (known as ketosis-prone T2DM) is increasing worldwide, with an incidence of 11% in children, whereas the incidence in adults is unknown.



Precipitating factors include infection, acute coronary syndromes, insulin omission or issues of pump malfunction

MECHANISMS

In T1DM and T2DM, insulin deficiency is accompanied by elevation of counter-regulatory hormones

Insulin deficiency leads to increased hepatic glucose production and reduced glucose uptake in peripheral tissues, leading to hyperglycaemia

Free fatty acids are oxidized in the liver to ketones

Glucose, ketones and free fatty acids

High levels of counter-regulatory hormones lead to increased lipolysis, releasing large quantities of free fatty acids, as well as reduced insulin action

Individuals with DKA exhibit deep and laboured breathing, often with a 'fruity' odour indicative of excess acetone

Accumulation of ketoacids decreases serum bicarbonate levels and leads to the development of metabolic acidosis

Severe hyperglycaemia and high ketone concentrations cause osmotic diuresis

DIAGNOSIS

DKA frequently presents with a short history, and symptoms — which include hyperglycaemia, polyuria and polydipsia — usually develop over a few hours. Abdominal pain is present in ~60% of patients; mental status and level of consciousness vary between individuals depending on the severity of hyperglycaemia and acidosis. Various international guidelines suggest that the presence of hyperglycaemia and acidosis and positive ketone tests confirm a diagnosis, although the methods of documenting ketosis (urine versus blood) vary.

The low pH due to acidosis can lead to neurological dysfunction, leading to coma and, if untreated, death

MANAGEMENT

The goal of therapy is to correct acidaemia, restore circulatory volume and normalize blood glucose concentrations and electrolyte disturbances. Most people are treated initially with intravenous insulin. A 'two-bag' method of fluid replacement is often used — intravenous fluid without dextrose initially and, upon volume correction, infusion with dextrose correction to prevent hypoglycaemia caused by the insulin therapy. Upon resolution of DKA and once patients are eating and drinking normally, maintenance therapy is implemented with subcutaneous insulin.

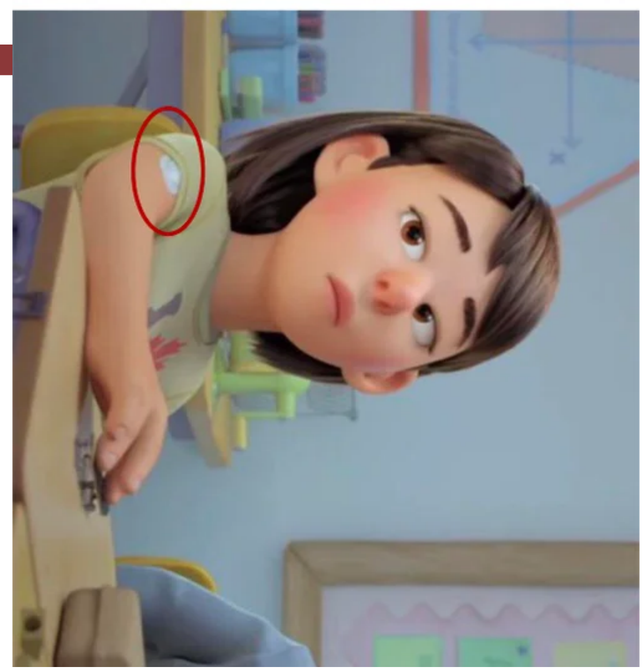
OUTLOOK

Several strategies have been proposed to reduce DKA events, including early screening, close follow-up of high-risk individuals (those with multiple admissions for DKA), availability of telephone support from diabetes specialist nurses and targeted programmes to educate parents and communities. In some parts of the world, efforts to ensure easy availability of insulin at an affordable price are needed.

doi:10.1038/s41572-020-0165-1

Written by Deepitha Maennich; designed by Laura Marshall

Tratamento



Bibliografia

BENALCÁZAR, S. et al. El uso de insulina en pacientes con diabetes tipo II. RECIAMUC, 2023.

CABRAL, A. C., et al. As Novas Insulinas: Oportunidades no Tratamento da Diabetes Tipo 1. Revista Portuguesa De Farmacoterapia, 2021.

Diabetic ketoacidosis. Nat Rev Dis Primers , 2020.

LI, F. et al. Higher glucose fluctuation is associated with a higher risk of cardiovascular disease: Insights from pooled results among patients with diabetes. J Diabetes, 2023.

LUCENA, J. B. S. Diabetes Mellitus Tipo 1 e Tipo 2. Trabalho de Conclusão de Curso – Curso de Farmácia da FMU. São Paulo, 2007.

PETERSON, S. Hyperglycemia in Pregnancy. STD.GOV Blog, 2018.

SILVERTHORN, D. U. Fisiologia Humana: Uma Abordagem Integrada. São Paulo: ARTMED EDITORA LTDA, 2017. p. 709-710

TODD, M.B. et al. Strategies for durable B cell replacement in type 1 diabetes. Science, 2021.