# HİPERGLİSEMİK HİPEROSMOLAR DURUM

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Acil Tıp Anabilim Dalı

# SUNUM PLANI

- Tanım
- Epidemiyoloji
- Patofizyoloji
- Klinik Özellikler (Öykü, Komorbidite, Fizik Muayene)
- Tanı ve Ayırıcı Tanı (Laboratuvar ve Görüntüleme)
- Tedavi (Sıvı Replasmanı, Elektrolit ve İnsülin)
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# The hyperosmolar hyperglycemic state (HHS) is a syndrome characterized by severe hyperglycemia, hyperosmolality, and dehydration in the absence of ketoacidosis

Diabetes Care 2014 Nov; 37(11): 3124-3131. http://dx.doi.org/10.2337/dc14-0984

## Hyperosmolar Hyperglycemic State: A Historic Review of the Clinical Presentation, Diagnosis, and Treatment

*Diabetes Care 2014;37:3124–3131 | DOI: 10.2337/dc14-0984*

*Francisco J. Pasquel and Guillermo E. Umpierrez*

**The hyperosmolar hyperglycemic state (HHS) is the most serious acute hyperglycemic emergency in patients with type 2 diabetes. von Frerichs and Dreschfeld described the first cases of HHS in the 1880s in patients with an "unusual diabetic coma" characterized by severe hyperglycemia and glycosuria in the absence of Kussmaul breathing, with a fruity breath odor or positive acetone test in the urine. Current diagnostic HHS criteria include a plasma glucose level >600 mg/dL and increased effective plasma osmolality >320 mOsm/kg in the absence of ketoacidosis. The incidence of HHS is estimated to be <1% of hospital admissions of patients with diabetes. The reported mortality is between 10 and 20%, which is about 10 times higher than the mortality rate in patients with diabetic ketoacidosis (DKA). Despite the severity of this condition, no prospective, randomized studies have determined best treatment strategies in patients with HHS, and its management has largely been extrapolated from studies of patients with DKA. There are many unresolved questions that need to be addressed in prospective clinical trials regarding the pathogenesis and treatment of pediatric and adult patients with HHS.**

The hyperosmolar hyperglycemic state (HHS) is a syndrome characterized by severe hyperglycemia, hyperosmolality, and dehydration in the absence of ketoacidosis. The exact incidence of HHS is not known, but it is estimated to account for <1% of hospital admissions in patients with diabetes (1). Most cases of HHS are seen in elderly patients with type 2 diabetes; however, it has also been reported in children and young adults (2). The overall mortality rate is estimated to be as high as 20%, which is about 10 times higher than the mortality in patients with diabetic ketoacidosis (DKA) (3–5). The prognosis is determined by the severity of dehydration, presence of comorbidities, and advanced age (4,6,7). Treatment of HHS is directed at replacing volume deficit and correcting hyperosmolality, hyperglycemia, and electrolyte disturbances, as well as management of the underlying illness that precipitated the metabolic decompensation. Low-dose insulin infusion protocols designed for treating DKA appear to be effective; however, no prospective randomized studies have determined best treatment strategies for the management of patients with HHS. Herein, we present an extensive review of the literature on diabetic coma and HHS to provide a historical perspective on the clinical presentation, diagnosis, and management of this serious complication of diabetes.

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**Table 1—From diabetic coma to HHS**

| Years | Authors (reference nos.) | Comment |
|---|---|---|
| 1828 | von Stosch (8) | Initial descriptions of diabetic coma |
| 1857 | Petters (10) | Discovery of acetone in the urine of patients with diabetes |
| 1865 | Gerhardt (91) | Discovery of acetoacetic acid in the urine of patients with diabetes |
| 1874 | Kussmaul (15) | First extensive description of diabetic coma |
| 1878 | Foster (11) | Cases of diabetic coma and acetonemia |
| 1883–1884 | Stadelmann (18)/Kölz (19)/Minkowski (20) | Discovery of β-hydroxybutyric acid in patients with diabetes |
| 1884–1886 | von Frerichs (21)/Dreschfeld (14) | Description of a nonketotic diabetic coma |
| 1922 | Banting et al. (83) | Insulin discovery |
| 1909–1923 | Lépine (92)/Revillet (93)/McCaskey (94)/Bock et al. (95) | Case series of diabetic coma without ketonuria |
| 1930–1935 | Lawrence (84)/Joslin (17) | Initial recommendations for the management of diabetic comas |
| 1957 | Sament and Schwartz (30)/de Graeff and Lips (29) | Detailed case reports of diabetic coma without ketones and hyperosmolality |
| 1962 | Singer et al. (85) | Linking osmolality and hyperglycemia |
| 1971 | Arieff and Carroll (55)/Gerich et al. (54) | Case series of HHS; initial criteria |
| 1973 | Arieff and Kleeman (77) | Mechanisms leading to cerebral edema |
| 1976–1977 | Alberti and Hockaday (60)/Kitabchi et al. (70) | Low-dose insulin protocols |
| 2004–2009 | Kitabchi et al. (4,86,87) | Position Statement, American Diabetes Association: management of hyperglycemic crises |
| 2011 | Zeitler et al. (59) | Guidelines for the management of HHS in children |

# HİPERGLİSEMİK HİPEROSMOLAR DURUM

- Progresif hiperglisemi ve hiperosmolarite
- Debil ve sıvı kısıtlaması olan kontrolsüz veya tanı almamış Tip 2 DM (genellikle) hastaları
- Genellikle eşlik eden veya kötüleştiren hastalık
- Genellikle yaşlı hastalar
- Komorbid hastalık veya metabolik hastalık
- Obez ve Afrikan amerikanlarda risk fazla

# PATOFİZYOLOJİ

1) İnsülin eksikliği veya direnci

2) İnflamatuvar durum ( proinflamatuvar sitokin → CRP, IL, TNF)

Hepatik glukoneogenez ve glikoneoliz artışı, **Önlenmiş lipoliz!!!**

3) Osmotik diürez ( bozulmuş glukoz atılımı ve TBW %20-25 kaybı)

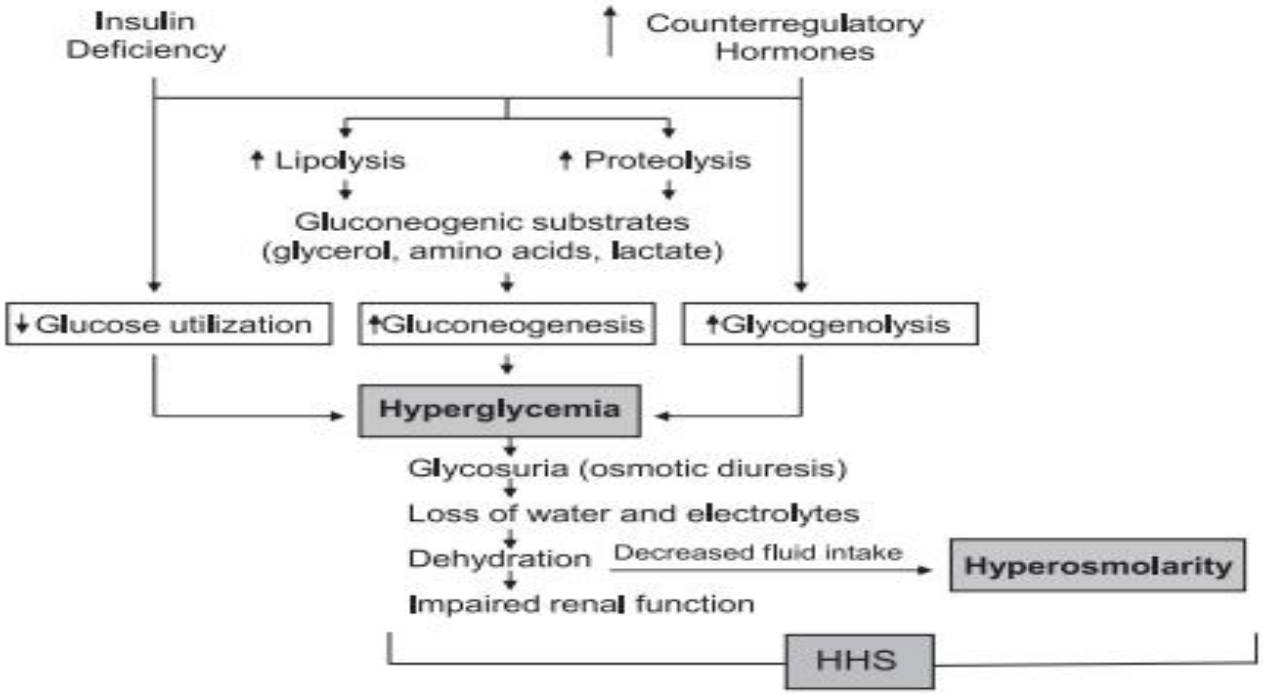


**Figure 1**—Pathogenesis of HHS.

# KLİNİK ÖZELLİKLER

- Gün - hafta içinde progresif mental durumda kötüleşme

- Nonspesifik vitaller ve bulgular (Ateş)

- Kuru membranlar
  Çökmüş gözler → osmolarite ve hiperglisemi
  Azalmış cilt turgor ciddiyeti ↑
  Hipotansiyon

- HHD'un %15'i acil servise nöbet ile başvurabilir (Genellikle fokal nöbet, nadiren jeneralize)

Seizure. 2010 Jul;19(6):359-62. doi: 10.1016/j.seizure.2010.05.006. Epub 2010 Jun 16.

# Occipital lobe seizures related to marked elevation of hemoglobin A1C: report of two cases.

Hung WL[1], Hsieh PF, Lee YC, Chang MH.

Author information

## Abstract

Occipital lobe seizures caused by nonketotic hyperglycemia (NKH) have been reported in only a few cases and are not fully characterized. We report two cases of NKH-related occipital lobe seizures with high hemoglobin A1C (HbA1C), epileptiform electroencephalograph (EEG) and MRI abnormalities. Both patients had moderate hyperglycemia (310-372 mg/dl) and mildly elevated serum osmolarity (295-304 mOsm/kg) but markedly elevated HbA1C (13.8-14.4%). One patient had a clinico-EEG seizure originating from the right occipital region during sleep. The other patient had an interictal epileptiform discharge consisting of unilateral occipital beta activity in sleep. None of the previously reported cases fulfilled the criteria of a nonketotic hyperglycemic hyperosmolar (NKHH) state, or showed any interictal beta paroxysms, spikes, sharp waves, or spike/sharp-slow wave complexes. We suggest that prolonged exposure to uncontrolled hyperglycemia, as indicated by HbA1C, rather than an acute NKHH state is crucial in the development of this peculiar seizure. We also suggest clinicians look for the presence of interictal focal beta paroxysms in addition to the usual epileptiform discharges while reading the EEG of these patients.

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PMID: 20558093 [PubMed - indexed for MEDLINE] **Free full text**

# KLİNİK ÖZELLİKLER

- Hipotermi → Kötü prognoz belirteci

- Yüksek osmolarite
  Ciddi hiperglisemi
  Asidoz → Koma riski ↑
  Ciddi hacim kısıtlaması
  Yaşlı hasta

# PREDİZPOZAN FAKTÖRLER

- Diyabet
- Miyokardiyal enfarktüs
- Pulmoner emboli
- Gastrointestinal kanama
- Pankreatit
- Mezenter iskemi
- İleri evre yanıklar
- Rabdomiyoliz
- Yapay beslenme desteği (parenteral veya enteral)
- Enfeksiyonlar, özellikle pnömoni veya üriner sistem enfeksiyonları
- Serebrovasküler olaylar
- Epilepsi
- Peritoneal veya hemodiyaliz
- Sıcaklık ilişkili hastalıklar
- Kokain kullanımı

Endocrinol Nutr. 2008 Oct;55(8):372-5. doi: 10.1016/S1575-0922(08)72799-2. Epub 2008 Dec 25.

## Hyperglycemia secondary to consumption of cocaine and atypical antipsychotic drugs.

[Article in English, Spanish]

Argente Villaplana CR[1], Civera Andrés M, Real Collado JT, Martínez-Hervás S, Ascaso Gimilio JF, Carmena Rodríguez R.

Author information

### Abstract

Drugs such as cocaine and atypical antipsychotic agents, such as olanzapine, are sometimes related to hyperglycemia. Whereas cocaine raises plasma glucose through catecholamine release, atypical antipsychotic agents mainly increase appetite and induce weight gain and the development of metabolic syndrome. Moreover, the latter group of drugs also act independently from weight gain or adiposity, due to inhibition of beta pancreatic cells and reduction of peripheral insulin action. We present the case of a 29-year-old non-diabetic woman with severe acute hyperglycemia in the context of a suicide attempt through intake of olanzapine and cocaine. After discontinuation of olanzapine and cocaine consumption, glycemia was immediately normalized without subsequent diagnosis of diabetes.

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PMID: 22975602 [PubMed]

Am J Geriatr Psychiatry. 2011 Dec;19(12):1026-33. doi: 10.1097/JGP.0b013e318209dd24.

## Antipsychotic drugs and the risk of hyperglycemia in older adults without diabetes: a population-based observational study.

Lipscombe LL[1], Lévesque LE, Gruneir A, Fischer HD, Juurlink DN, Gill SS, Herrmann N, Hux JE, Anderson GM, Rochon PA.

Author information

### Abstract

**OBJECTIVE:** To determine whether current antipsychotic use among older persons without diabetes is associated with a higher risk of hospital visits for hyperglycemia, as previous studies in this population have yielded conflicting results.

**DESIGN, SETTING AND PARTICIPANTS:** A nested case-control study within a population-based cohort of persons aged 66 years or older without diabetes, who initiated antipsychotic therapy between April 1, 2002, and March 31, 2006. Cohort members were identified using health databases from Ontario, Canada, and were followed from treatment start until March 31, 2007.

**MEASUREMENTS:** Cases were patients with a hospital visit (emergency department visit or hospital admission) for hyperglycemia. We matched each case with up to 10 controls. We compared the risk of hyperglycemia among current antipsychotic users to that of remote users (discontinued > 180 days).

**RESULTS:** The cohort consisted of 44,121 subjects, mean age of 78.3 years, followed for a mean of 2.2 years. Compared to remote antipsychotic use, current treatment with any antipsychotic was associated with a significantly increased risk of hospital visits for hyperglycemia (adjusted odds ratio [aOR]: 1.52; 95% confidence interval [CI]: 1.07-2.17). The risk was elevated for both atypical (aOR: 1.44; 95% CI: 1.01-2.07) and typical (aOR: 2.86; 95% CI: 1.46-5.59) antipsychotic agents.

**CONCLUSIONS:** Current use of either atypical or typical antipsychotic agents was associated with a significantly increased risk of hospital visits for hyperglycemia among older persons without diabetes. These findings highlight the need for close glucose monitoring during antipsychotic therapy in older populations.

PMID: 22123274 [PubMed - indexed for MEDLINE]

# PREDİZPOZAN İLAÇLAR

- Diüretikler
- Lityum
- Beta blokörler
- Mannitol
- Klorpromazin, Simetidine
- Glukokortikoidler
- İkinci jenerasyon antipiskotikler (ketiapin, ziprasidon)
- Fenitoin
- Kalsiyum kanal blokerleri

# TANI VE AYIRICI TANI

- Serum kan şekeri > 600mg/dl ( > 33.3 mmol/L)
- Kan pH > 7.3
- Serum HCO3 > 15meq/L
- İdrarda keton negatif veya +1 pozitif olabilir
- Plazma osmolalitesi > 315 mOsm/kg
- Laktik asidoz, açlık ketozu ve azotemi → pH ↓, ketonemi !!!

# TANI VE AYIRICI TANI
# Bilinç Değişikliği Yapan Durumlar

- Santral sinir sistemi enfeksiyonları
- Hipoglisemi
- Hiponatremi
- Hiperamonyemi
- Sepsis
- İntoksikasyon (etanol, narkotik…)
- Postiktal durumlar
- Aritmiler
- Hipotansiyon
- Akut kan kaybı
- Poliüri
- Aşırı diüretik kullanımı
- Diyabetes insipidus

# TANI VE AYIRICI TANI

| | DİYABETİK KETOASİDOZ | HİPERGLİSEMİK HİPEROSMOLAR DURUM |
|---|---|---|
| Plazma glukoz | > 250 mg/dL | > 600 mg/dL |
| Serum HCO3 | ≤ 18 mEq/L | > 15 mEq/L |
| İdrar asetoasetat | (+) | (-) veya düşük oranda |
| Serum keton | (+) | (-) veya düşük oranda |
| Serum osmolalite | Değişken | > 320 mOsm/kg |
| Anyon açığı | > 12 mEq/L | < 12 mEq/L |
| Arteryel/Venöz pH | < 7.30 | > 7.30 |

# LABORATUVAR

- Elektrolitler;
  - $Na^+$ → Hiperglisemi ile serum seviyesi ⬇ Pseudohiponatremi

    Düzeltilmiş $Na^+$ : Ölçülen $Na^+$ + $\frac{1,6 \text{ X (Glukoz -100)}}{100}$

    Glukoz > 400 mg/dL ise 2,4 ile çarpan kullanılır

  - $K^+$ → ⬇ Hacim kısıtlılığı ve asidemi durumunda !!! (geçici N)
  - $Mg^+$, $PO_4^{-3}$, → ⬇ Kardiyak ve sinir sistemi disfonksiyon
  - Osmolalite → ⬆ Ciddiyet ve koma durumu ile korele (> 320)

    Hiperglisemi durumunda osmolalite hesabı

    $2x\ Na^+ + glukoz/18 + BUN/2,8$

# TEDAVİ

- Doku perfüzyonunu sağlama
- Altta yatan sebeplerin tedavisi
- Elektrolit anormalliklerinin düzeltilmesi
- Hiperglisemi ve hiperosmolar durumun düzeltilmesi

# TEDAVİ
## Doku perfüzyonunu sağlama

- Hipovolemi düzeltilmesi
  - 8 - 12 L sıvı kaybı yerine koyulmalı (% 0.9 saline infüzyon ) (Na $^{+}$ düzeyi !)
  - Önce sıvı desteği ( ilk 12 saatte sıvı açığının yarısı) (15-20 mL/kg/st)
  - Taşikardi, hipotansiyon, üriner çıkış yeterli olunca %0,45 lik saline infüzyon

# TEDAVİ

## Altta yatan sebeplerin tanı ve tedavisi

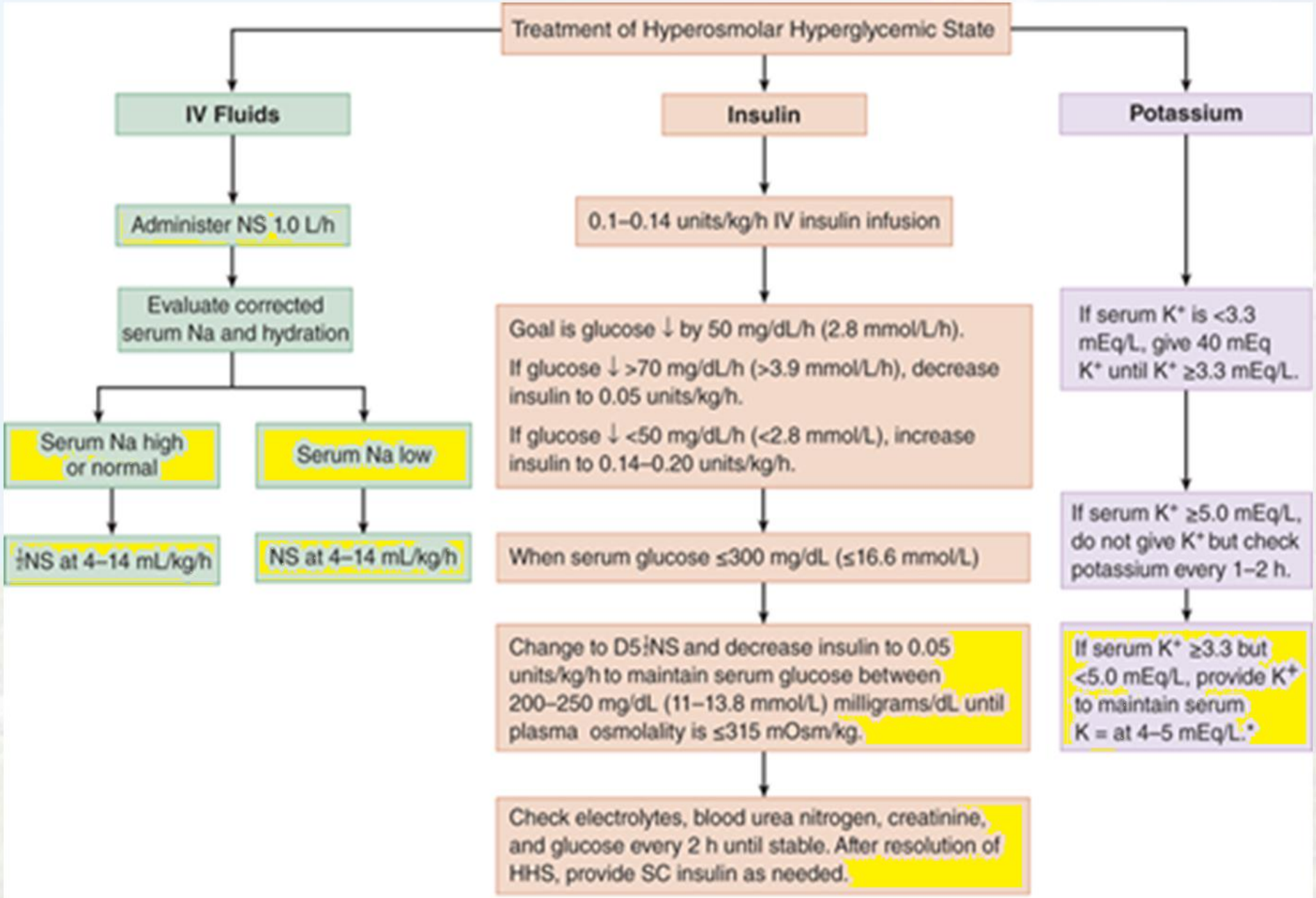
- Elektrokardiyogram
- Monitorizasyon
- Foley sonda
- Santral venöz yol
- Antitrombotik ilaçlar

# TEDAVİ
## Elektrolit anormalliklerinin düzeltilmesi

- $K^+ < 3,3$ mEq/L ise insülin başlamadan $K^+$ replasmanı yapılmalı!
- $K^+ \geq 20$ mEq/L desteği verilecek ise santral yol açılmalı!
- $Mg^+$ eksikliği → 1-2 gr > 1 st üzerinde infüzyon
- $PO_4^{-3} < 1,0$ mg/dL ise replase edilmeli, $KPO_4$ 2,5- 5 mg/kg > 6 st inf
- NaHCO3 desteği → eğer pH < 7,0 ise (100 mEq NaHCO3 400 mL saline inf)

# TEDAVİ
## Hiperglisemi ve hiperosmolar durumun düzeltilmesi

- Sıvı resusitasyonu sonrasında, intravenöz yol ile başla!
- 0,1 U/kg bolus ve 0,1 U/kg/st infüzyon
  (eğer ilk saat < %10 düşüş olursa ek doz!)
- Hedef → 50-75 mg/dL/st glukoz düşüşü
- Serum glukoz < 300 mg/dL olunca %5 dekstroz saline infüzyonuna geçiş, insülin infüzyon dozunu azalt !
- Hasta alert ve beslenebilecek düzeyde ise subkutan insülin düşün!




Source: Tintinalli JE, Stapczynski JS, Ma OJ, Cline DM, Meckler GD: *Tintinalli's Emergency Medicine: A Comprehensive Study Guide*, 8th Edition: www.accessemergencymedicine.com

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# KOMPLİKASYONLAR

- Beyin ödemi → Çocuklarda DKA'da ölümün > %50'sinden sorumlu iken erişkin HHD'da nadir!!

  Önlem için → İlk 4 saatte < 50 mL/kg SF yüklemesi

  Mental durum takibi

  Genel durum kötüleşme→ Beyin BT

  Ödem td → Mannitol (Osmotik tedavi sağlar)

  Mortalite → %12-42 arasında tedavi yanıtına göre değişir.

- Hipoglisemi
- Hipokalemi
- Pulmoner ödem (ARDS)

→ Abartılı resusitasyon ve yetersiz monitorizasyon

- Vasküler komplikasyonlar → Tromboembolizm, DIC

# Increased Risk of Ischemic Stroke after Hyperosmolar Hyperglycemic State: A Population-Based Follow-Up Study

**Jen-Yu Wang[1], Cheng-Yi Wang[1], Yung-Sung Huang[2], Pin-Fan Chen[3], Kuang-Yung Huang[4,5], Pesus Chou[6], Wei-Cheng Lian[3,4]*, Ching-Chih Lee[4,6,7,8,9]***

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## Abstract

***Background:*** Although much attention has been focused on the association between chronic hyperglycemia and cerebrovascular diseases in type 2 diabetes mellitus (DM) patients, there is no data regarding the risk of ischemic stroke after a hyperosmolar hyperglycemic state (HHS) attack. The objective of this study was to investigate the risk of ischemic stroke in type 2 DM patients after an HHS attack.

***Methods:*** From 2004 to 2008, this retrospective observational study was conducted on a large cohort of Taiwanese using Taiwan's National Health Insurance Research Database (NHIRD). We identified 19,031 type 2 DM patients who were discharged with a diagnosis of HHS and 521,229 type 2 DM patients without an HHS diagnosis. Using the propensity score generated from logistic regression models, conditional on baseline covariates, we matched 19,031 type 2 DM patients with an HHS diagnosis with the same number from the comparison cohort. The one-year cumulative rate for ischemic stroke was estimated using the Kaplan-Meier method. After adjusting covariates, Cox proportional hazard regression was used to compute the adjusted one-year rate of ischemic stroke.

***Results:*** Of the patients sampled, 1,810 (9.5%) of the type 2 DM patients with HHS and 996 (5.2%) of the comparison cohort developed ischemic stroke during the one-year follow-up period. After adjusting for covariates, the adjusted HR for developing ischemic stroke during the one-year follow-up period was 1.8 (95% C.I., 1.67 to 1.95, $P<0.001$) for type 2 DM patients with HHS compared with those without HHS.

***Conclusion:*** Although DM is a well-recognized risk factor for atherosclerosis, type 2 DM patients that have suffered a HHS attacks are at an increased risk of developing ischemic stroke compared with those without HHS.

# TABURCULUK VE TAKİP

- Debil ve komorbiditesi olan hastalar → ilk 24 saat yoğun bakım şartlarında gözlenmelidir

- Vital bulguları, idrar çıkışı, elektrolit dengesi ve mental durumu iyi olan hastalar kliniklerde takip edilerek kontrole çağrılır

# GÜNCEL YAYINLAR - VAKA

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Case Report

## Hamman syndrome: pneumomediastinum combined with hyperosmolar hyperglycemic state

**Abstract**

Although the causes for pneumomediastinum can be iatrogenic, postoperative, or traumatic, it is diagnosed as idiopathic when the apparent cause is not clear. In 1937, Hamman first described Hamman syndrome, which is pneumomediastinum combined with diabetic ketoacidosis (DKA). We describe a case of a 78-year-old man with a background of untreated diabetes mellitus that developed into hyperosmolar hyperglycemic state (HHS), which was complicated by pneumomediastinum. DKA and HHS are similar conditions that result in poor nutrition and Kussmaul breathing due to metabolic acidosis. These conditions could be involved in the pathogenesis of pneumomediastinum.

The patient, a 78-year-old man, had diabetes mellitus (DM) for which treatment was self-interrupted. The patient's neighbors found him collapsed with impaired consciousness, and he was transported in an emergency vehicle. At admission, his respiratory rate was 33 breaths per minute, $Spo_2$ was 95% (reservoir mask, 15 L/min), blood pressure was 110/55 mm Hg, pulse was 170 beats per minute and irregular, Glasgow Coma Scale was E3V3M5, and body temperature was 36.4°C. Based on the history of DM (hemoglobin A1c, 14.1%) and blood glucose of 577 mg/dL and negative urine ketones owing to loss of appetite for the previous few days, the cause of impaired consciousness was considered HHS, and appropriate volume expansion, glycemic control, electrolyte correction, and systemic management were conducted. Although the arterial blood gas analysis resulted in pH of 7.293, $Paco_2$ of 39.9 mm Hg, $HCO_3$ of 18.7 mEq/L, Glu of 517 mg/dL, Na of 136 mEq/L, K of 5.5 mEq/L, and Cl of 106 mEq/L at the time of hospitalization, the readings improved to 7.430, 40.1 mm Hg, 26.1 mEq/L, 129 mg/dL, 146 mEq/L, 4.0 mEq/L, and 114 mEq/L, respectively, on the second day of hospitalization. With treatment, consciousness improved to Glasgow Coma Scale of E4V4M6 on the fifth day of hospitalization. Although pneumomediastinum was observed on chest computed tomography (CT) at admission, it was considered idiopathic pneumomediastinum combined with HHS because pneumothorax and gastrointestinal perforations were not observed. We administered conservative medical treatment for pneumomediastinum (Figure). Upper gastrointestinal perforations were not observed in upper gastrointestinal tract endoscopy on the sixth day of hospitalization. A chest CT on the eighth day of hospitalization confirmed the disappearance of the pneumomediastinum. Subsequently, respiration and circulatory dynamics stabilized, and the patient was transferred after rehabilitation.

In this case, there were 2 important findings. Similar to Hamman syndrome, which is characterized by the combination of DKA and pneumomediastinum and first reported by Hamman in 1937 [1], pneumomediastinum and HHS were both present in the current case. Furthermore, the cause was considered the increased intrathoracic pressure—which is a mechanism of pneumomediastinum common to both DKA and HHS—that was caused by Kussmaul breathing and severe vomiting.

The routes for air to enter the mediastinum via leakage or penetration include the upper respiratory tract, intrathoracic airway, lung parenchyma, gastrointestinal tract, and sources external to the body [2]. Although the causes of pneumomediastinum can be iatrogenic, postoperative, or traumatic, it is considered idiopathic when the apparent cause is not clear. The frequency of idiopathic pneumomediastinum is 1 of 32,000 hospitalized persons [3]. Among the idiopathic conditions, the coexistence of pneumomediastinum and DM has been reported as Hamman syndrome [1]. In the present case, because the apparent cause was not obvious following the CT and endoscopic investigations, we determined that the pneumomediastinum was combined with HHS.

The pathogenesis of pneumomediastinum in DKA and that of pneumomediastinum in HHS could have similar mechanisms. Kussmaul breathing and poor nutrition caused by metabolic acidosis are involved in pneumomediastinum. There are various theories regarding the pathogenesis of Hamman syndrome. In one theory, free air leaking from the alveoli due to an increase in alveolar pressure caused by Kussmaul breathing and severe vomiting travels through the bronchovascular sheath and reaches the mediastinum from the pulmonary hilum [4]. In another theory, surface tension increases, and alveolar tissue elasticity decreases owing to a decrease in pulmonary surfactant because of marked malnutrition [5].

Similar to DKA, HHS causes Kussmaul breathing and poor nutritional status in many cases. Therefore, we considered that the Kussmaul breathing and malnutrition were involved in the development of pneumomediastinum. Pneumomediastinum can develop when there is a rapid increase in the intrathoracic pressure such as with repeated breathing during spirometry or strenuous exercises and repeated Valsalva maneuver breathing during childbirth or weight lifting.

In summary, a disease with combined pneumomediastinum and HHS exists. In this disease, Kussmaul breathing and malnutrition could be involved in the pneumomediastinum, similar to Hamman syndrome.

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Please cite this article as: Hirayama I, et al, Hamman syndrome: pneumomediastinum combined with hyperosmolar hyperglycemic state, Am J Emerg Med (2016), http://dx.doi.org/10.1016/j.ajem.2016.03.039

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DOI: 10.5527/wjn.v4.i2.319

World J Nephrol 2015 May 6; 4(2): 319-323
ISSN 2220-6124 (online)
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CASE REPORT

# Prolonged hypernatremia triggered by hyperglycemic hyperosmolar state with coma: A case report

Darlene Vigil, Kavitha Ganta, Yijuan Sun, Richard I Dorin, Antonios H Tzamaloukas, Karen S Servilla

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**Author contributions:** Vigil D and Ganta K contributed equally to this work; Vigil D and Ganta K were responsible for parts of the bibliographic search and of the first draft of the report; Sun Y and Dorin RI made critical changes in the manuscript; Tzamaloukas AH assisted in the bibliographic search and wrote parts of the original report; Servilla KS conceived the work and made critical changes in the manuscript.
**Ethics approval:** NA.
**Informed consent:** Approval for this case report was obtained from the human research committee of the Raymond G Murphy VA Medical Center.
**Conflict-of-interest:** The authors have no conflicts of interest to declare.
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**Received:** August 2, 2014
**Peer-review started:** August 2, 2014
**First decision:** October 14, 2014
**Revised:** January 7, 2015
**Accepted:** February 9, 2015
**Article in press:** February 11, 2015
**Published online:** May 6, 2015

## Abstract

A man with past lithium use for more than 15 years, but off lithium for two years and not carrying the diagnosis of diabetes mellitus or nephrogenic diabetes insipidus (NDI), presented with coma and hyperglycemic hyperosmolar state (HHS). Following correction of HHS, he developed persistent hypernatremia accompanied by large volumes of urine with low osmolality and no response to desmopressin injections. Urine osmolality remained < 300 mOsm/kg after injection of vasopressin. Improvement in serum sodium concentration followed the intake of large volumes of water plus administration of amiloride and hydrochlorothiazide. Severe hyperglycemia may trigger symptomatic lithium-induced NDI years after cessation of lithium therapy. Patients with new-onset diabetes mellitus who had been on prolonged lithium therapy in the past require monitoring of their serum sodium concentration after hyperglycemic episodes regardless of whether they do or do not carry the diagnosis of NDI.

**Key words:** Hypertonicity; Lithium; Hypernatremia; Hyperglycemia; Nephrogenic diabetes insipidus

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**Core tip:** Hyperglycemic coma with large losses of body water may aggravate lithium-induced nephrogenic diabetes insipidus (NDI) which had been asymptomatic and undiagnosed for years after cessation of lithium therapy. The development of conditions leading to loss of water and consciousness in patients who were on long term lithium therapy should trigger surveillance for NDI even when they were asymptomatic in the past.

Hindawi Publishing Corporation
Case Reports in Neurological Medicine
Volume 2014, Article ID 652523, 5 pages
http://dx.doi.org/10.1155/2014/652523

*Case Report*

# Osmotic Demyelination Syndrome as the Initial Manifestation of a Hyperosmolar Hyperglycemic State

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Received 11 August 2014; Accepted 15 October 2014; Published 9 November 2014

Academic Editor: José Luis González-Gutiérrez

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Osmotic demyelination syndrome (ODS) is a life-threatening demyelinating syndrome. The association of ODS with hyperosmolar hyperglycemic state (HHS) has been seldom reported. The aim of this study was to present and discuss previous cases and the pathophysiological mechanisms involved in ODS secondary to HHS. A 47-year-old man arrived to the emergency room due to generalized tonic-clonic seizures and altered mental status. The patient was lethargic and had a Glasgow coma scale of 11/15, muscle strength was 4/5 in both lower extremities, and deep tendon reflexes were diminished. Glucose was 838 mg/dL; serum sodium and venous blood gas analyses were normal. Urinary and plasma ketones were negative. Brain magnetic resonance revealed increased signal intensity on T2-weighted FLAIR images with restricted diffusion on the medulla and central pons. Supportive therapy was started and during the next 3 weeks the patient progressively regained consciousness and muscle strength and was able to feed himself. At 6-month follow-up, the patient was asymptomatic and MRI showed no residual damage. In conclusion, the association of ODS with HHS is extremely rare. The exact mechanism by which HHS produces ODS still needs to be elucidated, but we favor a rapid hypertonic insult as the most plausible mechanism.

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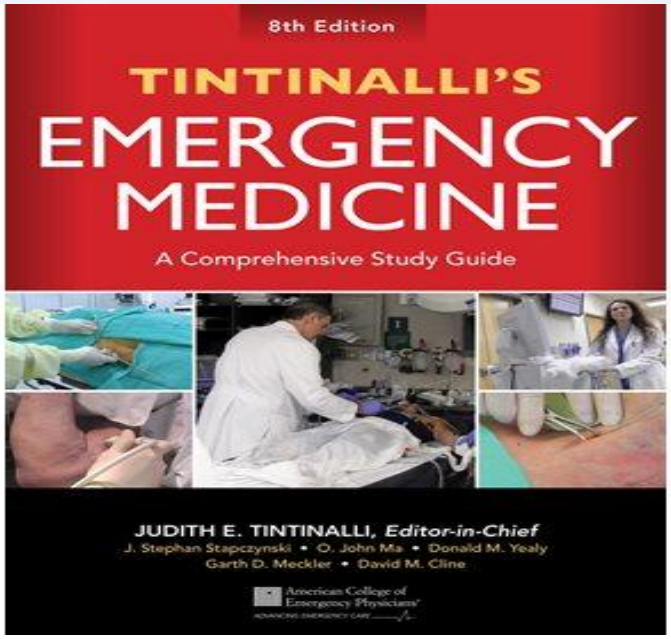
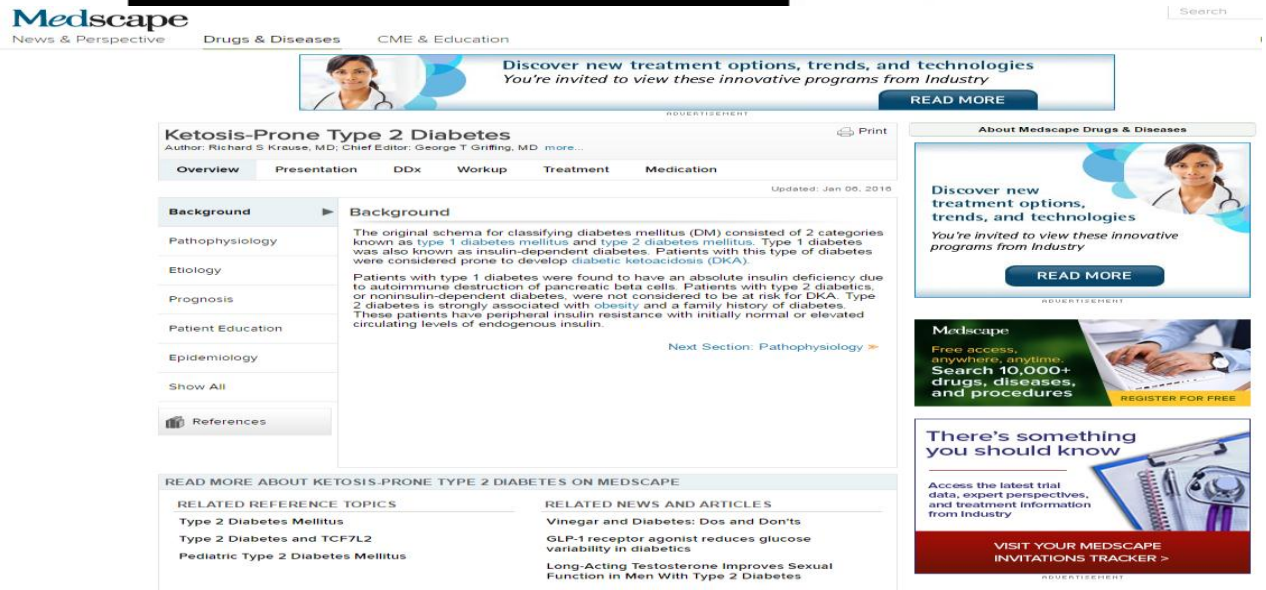
The National Diabetes Education Program (NDEP) works with partners to reduce the burden of diabetes and prediabetes by facilitating the adoption of proven approaches to prevent or delay the onset of type 2 diabetes and the complications of diabetes. NDEP is a joint program of the Centers for Disease Control and Prevention and the National Institutes of Health.

# KAYNAKLAR



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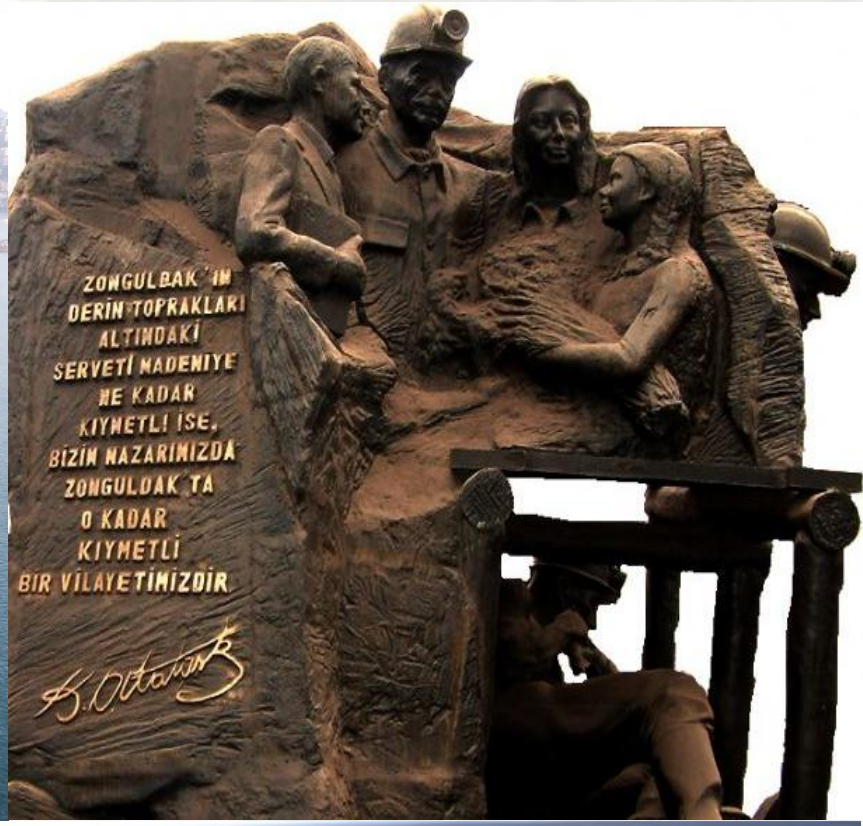
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