Brittle Diyabet: Nedenleri ve Tedavisi

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NEÜ Meram Tıp Fakültesi

- ‘The history of diabetes has been marked by recurrence of certain ideas which decline and disappear; only to go through a similar cycle again in an altered form in a new generation’

- Chicago physician R.T. Woodyatt 1934

A.Ç.

- 20 y, K
- 11 yaşından beri tip 1 DM
- İlk 2 yıl iyi kontrol sağlanabilirken, sonrasında KŞ düzensizlikleri gelişmiş. (Menarş)
- 9 yıl içerisinde 14 kez DKA tanısı ile hastaneye yatırılmış.
- Bu dönemde sık hipoglisemi atakları – bazen evde bazen hastaneye götürülmesini gerektiren

FM

- TA: 105/72 mmhg N : 82/dk ritmik.
- Kussmaul tipi solunum
- Tiroid palpasyonda düzensiz.
- Karın sol bölgesinde lipodistrofik alan
- Boy: 164cm, VA: 65 kg; BKİ: 25.5 kg/m^2
- Diğer bulgular N.

LAB.

Hb	11.3	**Na (mEq/L)**	128
BK (/mL)	7200	**K (mEq/L)**	3,2
BUN (mg/dL)	18	**Cl (mEq/L)**	99
Kreatinin (mg/dL)	0.9		
APG (mg/dL)	719	**ARTERYEL**	
HbA1c	11.2	**HCO3 (mEq/L)**	10
Sedim (mm/saat)	10	**pH**	7.1
		İDRAR KETON	++++

Takip

GÜN	SAAT	KŞ	Tdv	GÜN	SAAT	KŞ	Tdv
1	07.00	240	4 ü asp.	**2**	07.00	98	4
	10.00	100			10.00	476	
	12.00	350	4 ü asp.		12.00	145	4
	14.00	**40**			14.00	363	
	18.00	427	6 ü asp.		18.00	172	6
	20.00	254			20.00	199	
	22.00	217			22.00	93	
	24.00	113	12 Glar.		24.00	246	12
	02.00	156			02.00	220	

Brittle?

- Zor diyabet !
- Kırılgan - Oynak
- Labil
- Unstabil

- İnsülin mirası

- Tarihçe
- Tanım - Tanı
- Prevelans
- Sebepleri
- Tipleri
- Geçici mi?
- Tedavisi

Tanım

- **Woodyatt: 1930---**
- Bir hastada diğer sebepler dışlandıktan sonra hiperglisemi ve hipoglisemi arasında kırılgan seyreden insüline bağımlı diyabet

- Self replicating bibliografik virüs

Tanım

- **1977 Tattersal**

- Kan şekerlerinin sık ve öngürülemeyen şekilde hipoglisemi ve /veya ketoasidoza yol açarak hayat kalitesini bozacak şekilde düzensiz seyretmesi

Brittle

- Öngörülemeyen epizodlar hemen hemen her zaman endojen insülin yokluğuna bağlı
  C peptid<
- Tip 1 diyabetikler
- Kan şekerinde geniş dalgalanmalar olan, aynı tip ve aynı doz insülin tedavisine, farklı kan şekeri cevapları veren hastalar

Tanı?

- 4 yıllık bir zaman dilimi içinde en az 3 kez diyabetik ketoasidoz nedeniyle hospitalizasyon ihtiyacı doğması
  - Gill
- 2 yıl içinde 3 kez
  - Tattersal
- Bir yıl içinde 3 kez hipoglisemiye bağlı yatış

Objektif Değerlendirme

- **MAGE**: Mean Amplitude of the largest Glycemic Excursions (20-60 mg/dl)
- **MODD**: Mean Of Daily Differences (160)
- **LI**: Lability Index
- **LBGI**: Low Blood Glucose Index >5
- **Clarke's score** >4
- **Hyposcore**
- Continuous blood glucose monitoring system

Prevelans

- BD prevelansı; 1-1.2 / 1000 diyabetik hasta
- İnsülin kullanan hastaların 1-3 /1000 hasta

AMA

- Bireye, aileye, sağlık personeline ciddi sorun, ekonomiye de sık yatış gerekliliği sebebiyle ek maliyet

- Sağlık personelinde motivasyon-moral kaybı


Moralim bozuk değil de sanki böyle çürümüş gibi, küflenmiş gibi, ölmüş gibi.

Maliyet

- BD hasta için yılda 1500 $, diyabetli için yılda 564 $
- Reküren DKA ya da hipoglisemi nedeniyle hastane başvurularının > %90

BD Tipleri

- **Rekürren hiperglisemi %59** ;
  - rekürren DKA, son 2 yılda 3 ya da daha fazla, daha çok genç hastalarda, obez kadın, insülin enjeksiyonlarında kompliyans sorunu

- **Rekürren hipoglisemi %17** ;
  - yılda en az 3 epizod daha çok ileri yaşta

- **Mikst glisemik değişkenlik % 24,**
  - daha çok ileri yaşta

Sebepler

- Subkutan insülin direnci,
- Bozulmuş insülin emilimi,
- Artmış insülin klerensi,
- İnsülin injeksiyon yerlerinin değiştirilmemesi (lipohipertrofiler)
- Bir defada yapılan insülin dozunun yüksek olması (insülinin absorpsiyonu yavaşlar, pik etki gecikir ve etki süresi değişir),
- Hastanın tükettiği karbonhidrata uygun insülin dozunu belirleyememesi,
- Kullanılan glukometre veya striplerden kaynaklanan hatalar (kalibrasyonu yapılmamış alet veya miyadı geçmiş strip v.b.),
- Fibrokalküloz pankreatik diyabet,
- İatrojenik ya da faktisiyöz sebepler,
- Otonomik nöropati,
- Gastroparezi,
- Çölyak hastalığı,
- Hipogliseminin farkında olamama durumu,
- Psikiyatrik sebepler

Yaş

- 15-30’lu yaşlarda zirve, daha küçük zirve ise 60-70’li yaşlarda

A.Ç.

- Fluoksetine tdv 2 yıldır alıyor
- Psikiatri kontrolü
- Pompa…
- 8 ayda iki kez DKA, bir kez hipoglisemi

Journal of the Royal Society of Medicine Volume 85 May 1992

The spectrum of brittle diabetes

G V Gill FRCP DTM&H *The Diabetes Centre, Walton Hospital, Rice Lane, Liverpool L9 1AE*

Keywords: insulin-dependent diabetes; brittle diabetes; hypoglycaemia

Sub-group	*Definition*	*Frequency*
Recurrent ketoacidosis	90% or more of admissions due to DKA	n=22 (52%), all female
Hyperglycaemic instability	90% or more of admissions due to hyperglycaemic instability, but DKA uncommon	n=10 (24%) 4 f/6 m
Recurrent hypoglycaemia	90% or more of admissions due to hypoglycaemia	n=5 (12%), 3 f/2 m
Mixed instability	Hypo and hyperglycaemic admissions with no clear pattern	n=5 (12%), all female

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Table 2. Characteristics of brittle diabetic patients compared with a control group of 'stable' diabetics (means±SD)

	Brittle (n=*42*)	*Stable* (n=*42*)	
Sex ratio	6 m/36 f	19 m/23 f	$P<0.01$
Age (years)	27.9±12.8	40.1±13.6	$P<0.001$
Duration of diabetes (years)	13.7±9.4	19.6±11.2	$P<0.01$
HbA_1 (%)	13.7±3.1	10.1±1.5%	$P<0.001$
Insulin dose (u/day)	98±81	47±14	$P\ll0.001$
Complications	18 (43%)	15 (36%)	NS
Psychosocial problems	31 (74%)	7 (17%)	$P\ll0.001$

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Table 3. Psychosocial disturbances amongst brittle diabetic patients and stable controls

Psychosocial problem	*Brittle group (n=42)*	*Stable group (n=42)*
Family disturbances	12	1
Adolescent crises	7	0
Personality disturbances	7	3
Depression	6	3
Anorexia nervosa	3	1
Self-destructive behaviour	3	0
Anxiety	1	2
Total	39 (in 31 patients)	10 (in 7 patients)

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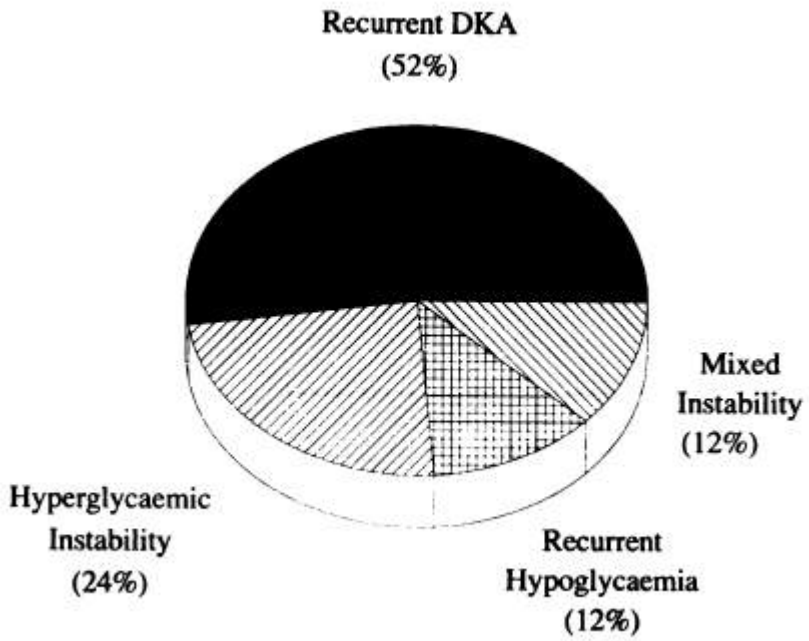

Değerlendirme

- Anamnez; diyabet süresi
- Ortaya çıkış zamanı
- Tetikleyen bir olay
- İnsülin tedavisi
- Diyabet komplikasyonları; otonomik, gastroparezi,
- Psikososyal faktörler

BRITTLE DM TEDAVİSİNDE ESKİ YÖNTEMLER (1922-1950)

- Hipofizektomi
- Hipofize yönelik radyoterapi
- Adrenalektomi

Houssay et al. Endocrinology, 1931; 15: 511-23
Long et al. Ann Int Med; 1936; 9: 1619-27

Tedavi

- Deneyimli ekip
- Eğitim!
- Sık KŞ takibi
- Psikososyal değerlendirme
- Çoklu insülin tdv
- İnsülin pompası
- Adacık-pankreas nakli

Hiperglisemi-DKA

Organik sebepler

- Obezite, sedanter yaşam
- Yaş-Puberte(kızlar)
- Kronik enfeksiyonlar-Tbc,apse
- Endokrinopatiler
  - Hipertiroidi
  - Akromegali
  - Feokromasitoma
  - Cushing's sendromu
- İlaçlar
  - Glukokortikoid
  - Beta agonistler

İnsülin etkisindeki bozukluklar (çok nadir)

- Antikorlar
- Hızlanmış insülin yıkımı
- İnsülin reseptör ilişkili problemler

Psikososyal etkenler

•Psikiatrik hastalıklar
•İnsülin atlama ve düzgün kullanmama
•Diyabetle yaşamada başarısızlık

M.A.

- 69 yaşında kadın
- 3 yıllık diyabet, tanıdan itibaren insülin
- KLL - remisyonda 5 yıl
- Bazal-bolus tdv kullanıyor (mu?)
- Acil servise
  - KŞ: 820 mg/dl, keton +++, pH: 7.28
- İYE

M.A. - FM

- Boy: 162 VA: 92 kg VKİ: 35
- TA: 125/84 mmhg
- Genel durumu iyi
- Son 6 ayda 9 kez acil servis başvurusu-DKA
- Daha önce 4 kez poliklinik başvurusu
- Tek başına yaşıyor – evde kızı yardım ediyor

M.A. - LAB

- A1c: % 10.2
- Tam kan normal
- Elektrolitler normal
- 2 gün önce acil servis
- Dün servis
- Her zaman 24-48 saatte kan şekerleri regüle

- Which is Unstable—the Patient or the Diabetes?

- **Dr. Joslin 1956**

Hipogliseminin organik sebepleri

- Endokrin hastalıklar
  - Addison
  - Hipotiroidi
  - Pitüiter yetmezlik
- İlaçlar
- Bağırsak ve pankreas hastalıkları
- Hipoglisemik farkındasızlık

A.A.

- 29 yaşında, 11 yıllık diyabetik- Tip 1
- 9 ay önce günlük 44 ü insülin; A1c: %7.4
  - 3x10 ü aspart, 24 ü glargine
- Son 2 ayda 5 kez hipoglisemi nedeniyle acil servis başvurusu, son ikisinde ciddi
- İlk hipoglisemi futbol maçı sonrası-daha önceden olmayan
- Son 5 ayda 6 kg vermiş, hayatında değişiklik yok

A.A.

- İnsülin dozları 26 ü kadar düşürülmüş
- Son A1c: % 6.6, fazladan insülin yapmadığını belirtiyor.
- TA: 96/68 mmHg, kre: 1.1 mg/dl, Na: 128 mmol/L, K: 5.1 nmol/L

- ACTH: 182 ng/dl (10-80)
- Kortizol: 2.8 μgr/dl
- Prednizolon başlandı: ihtiyaç 36ü/gün
- 4 kg almış, ihtiyaç 46ü/gün: Hipoglisemi yok

Pankreas yoksa-hipoglisemi

- Çünkü glukagon da yok
- 58 mg/dl; çarpıntı, titreme, güçsüzlük, görme problemleri, açlık
- 54 mg/dl; halsizlik, sersemlik, konfüzyon
- 50 mg/dl; kognitif bozukluk, koma
- Rakamlar bireysel farklılıklar gösterebilir (glisemik kontrol kötüyse)

Hipogliseminin farkında olamama

- İnsülinle tdv sonrası; 25 yıl sonra %50 oranında görülüyor
- Sebep; multifaktöriyel
  - Hipotalamus ve arkabeyindeki nöronlar
  - Periferik glukoz reseptörleri-Kc portal sistem
  - Periferik otonomik nöropati-azalmış epinefrin cevabı(otonomik semptomları engelleyerek ya da şiddetini azaltarak)

Hipogliseminin farkında olamama

- Hafif tek hipoglisemi epizodu: Bir sonraki hipoglisemiye cevabı;
- Sempatik ve nöroendokrin cevapları 24 saate kadar azaltabilir
- **Fasit daire-kısır döngü**
- Kötü glisemik kontrollü hastalarda, normo-hiperglisemik değerlerde bile hipoglisemik semptomlar,
- Hipoglisemi: algı ⟶ dökümante edilmeli

Psikososyal faktörler (74%)

Malabsorpsiyon
- Çölyak hastalığı
- Yağ malabsorpsiyonu

İlaçlar
- Alkol
- Antipsikotik ilaçlar (Quetiapine)

Otonomik nöropati
- Gastroparezi
- Hipogliseminin farkında olamaması

Subkutan sebepler
- Bozuk insulin emilimi
- Hızlanmış yıkım
- İnsulin allerjisi

Kontroregülatuar hormonlardaki defektler
- Adrenal yetmezlik
- Hipopituitarizm
- Glukagon eksikliği (eg. Post-pankreatekomi)
- Anormal BH regülasyonu

Oto-antikorlar
- Anti-insulin
- Anti-insulin reseptör

Management strategies for brittle diabetes. M.-C. Vantyghem , M. Press. Ann. Endocrinol., 2006

- Depresyon prevelansı Tip 1 diyabetiklerde %11 hayat boyu risk ise %25

Course of brittle diabetes: 12 year follow up

Robert Tattersall, Robert Gregory, Colin Selby, David Kerr, Simon Heller

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BMJ 1991;302:1240-3

TABLE I—*Details of brittle diabetic patients and matched controls*

	Recurrent hypoglycaemia group	Control group	Recurrent ketoacidosis group	Control group
No of patients (males/females)	12* (6/6)	24 (12/12)	10† (5/5)	20 (10/10)
Median (range) age at diagnosis of diabetes (years)	12 (5-25)	12 (10-26)	10 (2-40)	10 (1·6-41)
Median (range) duration of diabetes in 1989-90 (years)	21 (14-45)‡	20 (13-46)	19 (11-22)	17 (11-23)
Total No of admissions with hypoglycaemia	237	10	20	22
No of patients admitted with hypoglycaemia	12	8	6	9
Total No of admissions/patient (range)	6-40	0-2	0-8	0-8
No of admissions with hypoglycaemia/year of diabetes§	0·83	0·02	0·12	0·07
Total No of admissions with ketoacidosis	75	11	292	23
No of patients admitted with ketoacidosis	8	7	10	11
Lifetime admissions/patient (range)	0-26	0-2	8-67	0-4
No of admissions with ketoacidosis/year of diabetes§	0·26	0·02	1·69	0·07

Case 1—This man had developed diabetes at age 5 and between the ages of 14 and 17 was admitted to hospital 30 times. No cause was found for any of these episodes, recovery was swift, and it became obvious that he enjoyed being in hospital and disliked school and home. After he left school and home in 1979 he was admitted to hospital only twice, once for abdominal pain and once for an insulin overdose after his wife left him. Control of his diabetes was poor (haemoglobin A_1 concentration 12·5%), but his only complication was background retinopathy. In retrospect, his sister, who had developed diabetes a year before his brittleness began, believed that it was deliberately induced to obtain his mother's attention, though he attributed it to a need to escape from his parents' marital disharmony.

Case 2—A mother with six children developed diabetes aged 40 and started insulin four years later because of tablet failure. Between 1977 and 1985 she was admitted 30 times with ketoacidosis, 21 times on a Friday or Saturday coinciding with weekends when her husband came home. She had often been seriously ill when admitted and it was agreed that she should refer herself to the diabetes ward if she needed a rest. After her divorce in 1986 admissions fell from five to two a year and the duration of each admission from an average of five to two days.

Case 3—A daughter of West Indian parents developed diabetes at age 10. Four years later, during which time she had been admitted to hospital four times with ketoacidosis, she was thought to be seriously depressed. However, her parents refused to allow her to see a psychiatrist. From age 15 to 19 she had 52 admissions with ketoacidosis, took three overdoses of analgesics, performed reasonably well in school examinations, and lost her only confidant at home when her elder brother was sent to prison. She admitted that all her admissions were precipitated by omitting insulin and said several times, "If you send me home, I'll kill myself." Discussion of her problems was repeatedly blocked by her parents' refusal to discuss the situation. After 1982 she trained as a nurse and was admitted once with ketoacidosis, once with hypoglycaemia, and several times with other problems.

TABLE II—*Clinical outcome in 1989-90 of 22 patients in whom brittle diabetes was diagnosed in 1977-9 and 44 matched controls*

	Recurrent hypoglycaemia group	Control group	Recurrent ketoacidosis group	Control group
No of patients	12	24	10	20
No of patients (No of admissions) in past 2 years with hypoglycaemia	7 (13)	1 (1)*	1 (1)	1 (2)
No of patients (No of admissions) in past 2 years with ketoacidosis			5 (9)	1 (1)†
Median (range) last haemoglobin A_1 concentration (%)	9·3 (7·9-14·2) (n=10)	10·3 (6·5-13·9) (n=21)	14·0 (8·8-15·9) (n=6)	11·8 (7·4-14·6) (n=17)
Median (range) insulin dose (U/kg/day)	0·70 (0·40-1·02)	0·73 (0·26-1·12)	0·95 (0·62-2·14)	0·90 (0·42-1·25)
No who died	2	1	1	
No (%) with microvascular complications:				
None	5 (42)	8 (33)	1 (10)	5 (25)
Background retinopathy	3 (25)	10 (42)	6 (60)	10 (50)
Proliferative retinopathy	4 (33)	6 (25)	3 (30)	4 (20)
Proteinuria	1 (9)	2 (8)	1 (10)	2 (10)
No (%) employed	9 (75)	22 (92)	8 (80)	19 (95)
No (%) married	6 (50)	19 (79)	4 (40)	9 (45)

Conclusion

Only two patients, both with end stage diabetic nephropathy, had an organic cause for brittle diabetes. In the rest instability was due to behavioural or social factors. Admission rates for both groups fell greatly over the 12 years of follow up, and in 1989-90 only one patient from each group would have fulfilled the original inclusion criteria. Nevertheless, admission rates for both hypoglycaemia and ketoacidosis remain significantly higher than those in the control groups. Though no patient in the ketoacidosis group had died as a result of diabetes, two in the recurrent hypoglycaemia group had died of hypoglycaemia. The prevalence of complications in patients with brittle diabetes, whether hypoglycaemic or ketoacidotic, was comparable with that in patients whose diabetes had never been brittle.

Prevalence and characteristics of brittle diabetes in Britain

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Table 1 UK prevalence rates of brittle diabetes

Returned figures	
1. Total brittle diabetic patients	414
2. Number of clinics	432
3. Total diabetic patients	354 824
4. Total diabetic patients on insulin	143 193
Prevalence rates	
1. Brittle patients per clinic	1.0 per clinic
2. Per total diabetic patients	1.2 per 1000
3. Per insulin-treated diabetic patients	2.9 per 1000

Hastaların sadece 18’inde (%7) organik sebepler saptanmış. Bunlar:

-Otonomik nöropati (5)
-Subkutan insülin direnci (3)
-Demans (3)
-Mental bozukluk (2)
-Çölyak hastalığı (2)
-KBY (1)
-Hipopituitarizm (1)
-Steroid tdv (1)

Mikst glisemik değişkenlik %24

- Rekürren enfeksiyonlar (İYE, ÜSYE, sinüzit, tonsilit, PİD)
- Endokrinopatiler (kontroregülatuar hormonların salınımında bozukluk, hipoadrenalizm, glukagon yetersizliği)
- Uygun olmayan insülin rejimi ve zamanlaması, hipogliseminin aşırı tdv edilmesi, egzersizin gecikmiş etkisi, alkol
- Psikososyal problemler

A.D.

- 52 yaş, erkek
- 22 yıllık diyabet
- Retinopati – nefropati – periferik simetrik sensorinöral polinöropatisi mevcut
- Sık hipo-hiperglisemileri var
- Bazal-bolus tdv alıyor

A.D. - FM

- Boy: 171 cm VA: 75 kg VKİ: 25.6
- TA: 105/68 mmhg N: 92/dk
- Ortostatik hipotansiyonu var
- Alt ekstremetilerde basınç, ağrı, vibrasyon duyuları tibia ortasına kadar kaybolmuş
- Diğer sistem muayenelerinde patoloji yok

A.D. - LAB

- AKŞ: 278 mg/dl A1c: % 9.6
- Kre: 1.6 Na: 132
- TSH: 3.2

KŞ Takibi

Zaman	Kan şekeri mg/dl	Tdv	
06	145	4ü aspart	Kahvaltı
08	52		
10	380		
12	183	6ü aspart	Öğle yemeği
14	78		
16	302		
18	284	8ü aspart	Akşam yemeği
20	65		
22	320	20ü glarjin	
24	168		
02	102		
04	135		

Ne yaparsınız?

- Mide boşalma zamanı 105 dk
- Domperidon: fayda yok
- Tedavi?
  - Hızlı etkili analog – zamanı
  - Kristalize insülin – zamanı
  - Gastrik pacemaker
  - Gastrostomi ?

- We must not forget in treating diabetes that we are treating a man and not a disease

- Francis Peabody 1984

- Erişkin Çölyak hastalarının %19'u 60 yaş ve üzerinde
- BD ile beraber Fe eksikliği anemisi varsa Çölyak dışlanmalı

The outcome of brittle type 1 diabetes—a 20 year study

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- 10’u (%50) 20 yıl içinde vefat etmiş

- Sağ kalan 10 kişiden hiçbirinde DM oynak seyretmemiş, ancak hepsinde de diyabet komplikasyonları yoğun gelişmiş!
  - Nefropati veya mikroalbuminuri % 70
  - Retinopati % 90
  - Nöropati % 100

The outcome of brittle type 1 diabetes—a 20 year study

A. CARTWRIGHT[1], M. WALLYMAHMED[1], I.A. MACFARLANE[1], A. WALLYMAHMED[2], G. WILLIAMS[3] and G.V. GILL[1,4]

Table 3 Complications of brittle diabetic patients compared with case–controls

	Brittle ($n=10$)	Controls ($n=20$)	Significance
Nephropathy			
None	3	15	
Microalbuminuria	1	2	
Proteinuria	2	3	
Renal impairment	3	0	
End-stage renal failure	1	0	
Total renal disease	7	5	$P<0.05$
Retinopathy			
None	1	3	
Retinopathy no laser	1	12	
Retinopathy with laser	6	5	
Partially sighted	1	0	
Registered blind	1	0	
Total retinopathy	9	17	p NS
Peripheral neuropathy			
None	3	14	
Diagnosed neuropathy (no treatment)	3	5	
Diagnosed painful neuropathy (treated)	4	1	
Total peripheral neuropathy	7	6	pNS (0.56)

The outcome of brittle type 1 diabetes—a 20 year study

A. CARTWRIGHT[1], M. WALLYMAHMED[1], I.A. MACFARLANE[1], A. WALLYMAHMED[2], G. WILLIAMS[3] and G.V. GILL[1,4]

Autonomic neuropathy			
None	5	20	
Gastro-paresis	4	0	
Postural hypotension	1	0	
Total autonomic neuropathy	5	0	$P<0.002$
Large vessel disease			
None	9	17	
IHD	1	1	
CVD	0	1	
PVD	0	1	
Total	1	3	pNS

The outcome of brittle type 1 diabetes—a 20 year study

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Table 4 Demographic and other data among the brittle survivors ($n = 10$), and the non-brittle case–controls

	Brittle ($n = 10$)	Case–controls ($n = 20$)	Significance
Age (years)	42 ± 4	46 ± 6	NS
Duration (years)	32 ± 5	30 ± 6	NS
BMI (kg/m^2)	28.3 ± 4.6	30.0 ± 5.4	NS
HbA1c (%)	9.4 ± 1.5	8.8 ± 1.0	NS
Cholesterol	4.3 ± 0.4	4.5 ± 0.9	NS
HDL cholesterol	1.8 ± 0.4	1.6 ± 0.4	NS
Insulin dose (u/day)	51 ± 33	59 ± 33	NS

Results expressed as mean ± SD; NS, not significant.

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Table 1 Causes of death among 10 brittle type 1 diabetic patients during 20 years of follow-up

CRF	3
DKA	3
Hypoglycaemia	2
Subarachnoid haemorrhage	1
Uncertain	1

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Table 2 Details of the brittle cohort at baseline and at 10 and 20 years follow-up

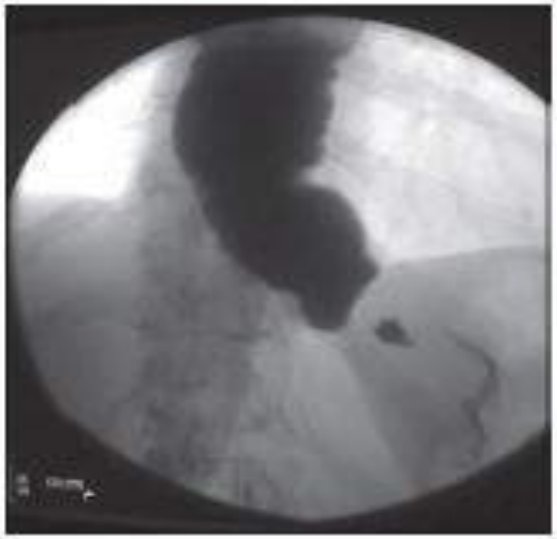
	Initial study 1979–81, ($n=33$)	Follow-up (1) 1991–92, ($n=20$)	Follow-up (2) 2005–06, ($n=10$)
Age (years)	18 ± 5 (12–44)	29 ± 6 (22–44)	42 ± 4 (36–50)
Duration of diabetes (years)	8 ± 4 (2–19)	18 ± 5 (10–31)	32 ± 5 (24–40)
Number of brittle (%)	21 (100)	2 (10)	0 (0)
Diabetic complications (%)	0 (0)	14 (67)	10 (100)
BMI (kg/m^2)	24.7 ± 3.2	25.1 ± 3.5	28.3 ± 4.6[a,b]
Insulin dose (u/day)	124 ± 55	77 ± 39[c]	51 ± 33[a,b]
Admissions in last year (mean per person)	12	2	0
DKA in last year (mean per person)	8	1	0

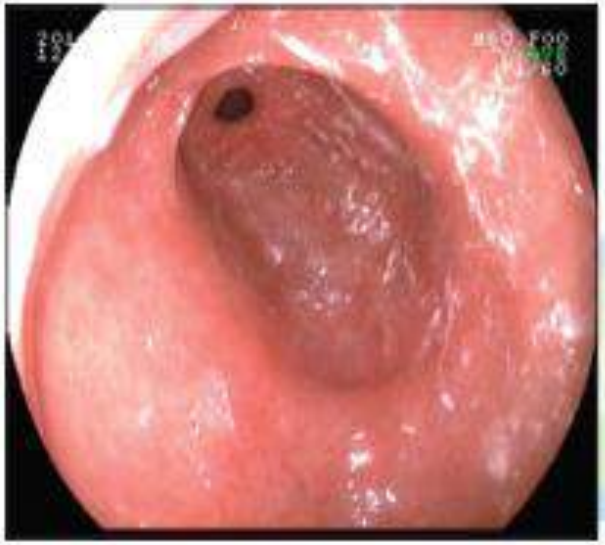
Results expressed as mean ± SD (range) or actual number (%). [a]$P<0.01$ initial vs. follow-up (2). [b]$P<0.05$ follow-up (1) vs. follow-up (2). [c]$P<0.01$ initial study vs. follow-up (1).

Brief Communication

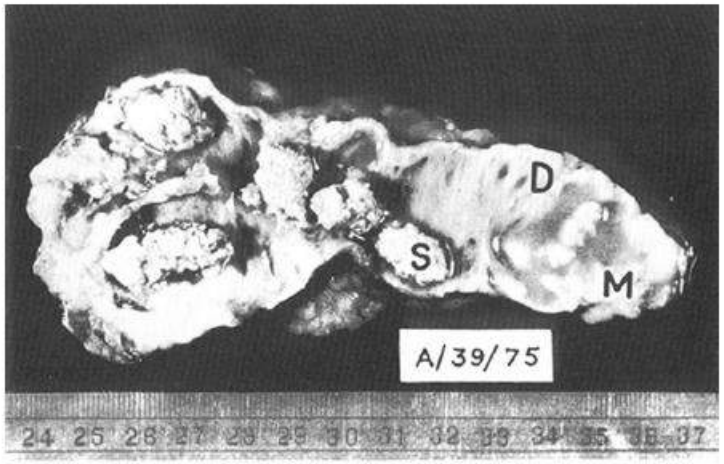
Brittleness of diabetes due to achalasia cardia managed successfully by multiple innovative strategies

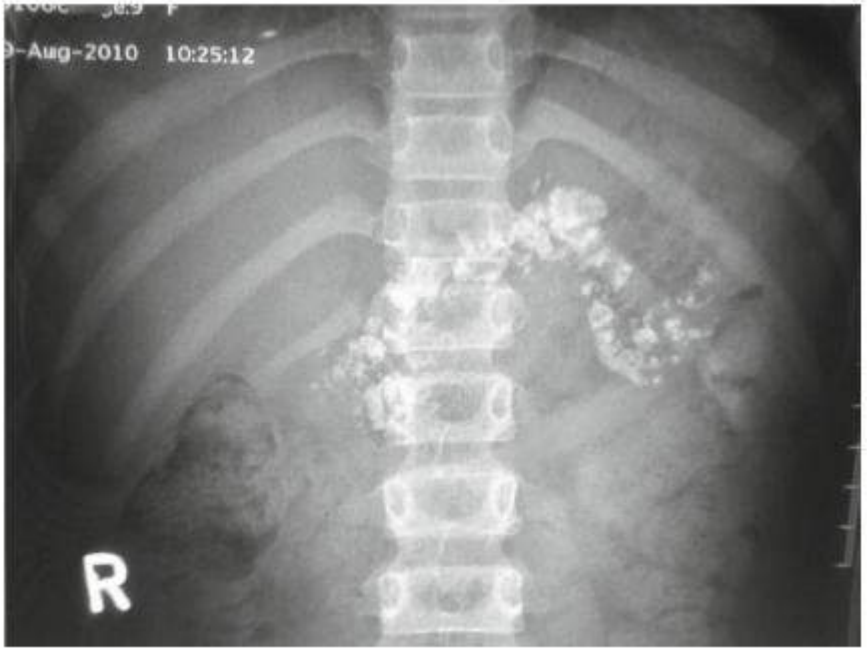
Vimal Upreti, Rohit Vashist[1], Pavan Dhull[2], V. R. Mujeeb[2], M. S. Prakash[1]
Departments of Endocrinology, [1]Medicine, [2]Neurology, and [3]Gastroenterology, Command Hospital (Air Force), Bangalore, Karnataka, India





Fibrokalküloz pankreatik diyabet





Pergamon

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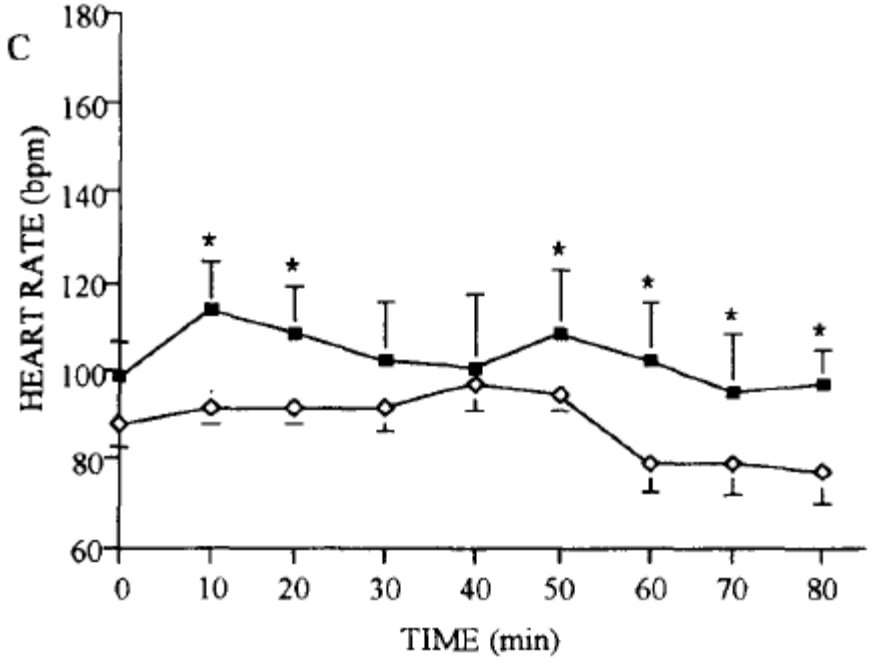
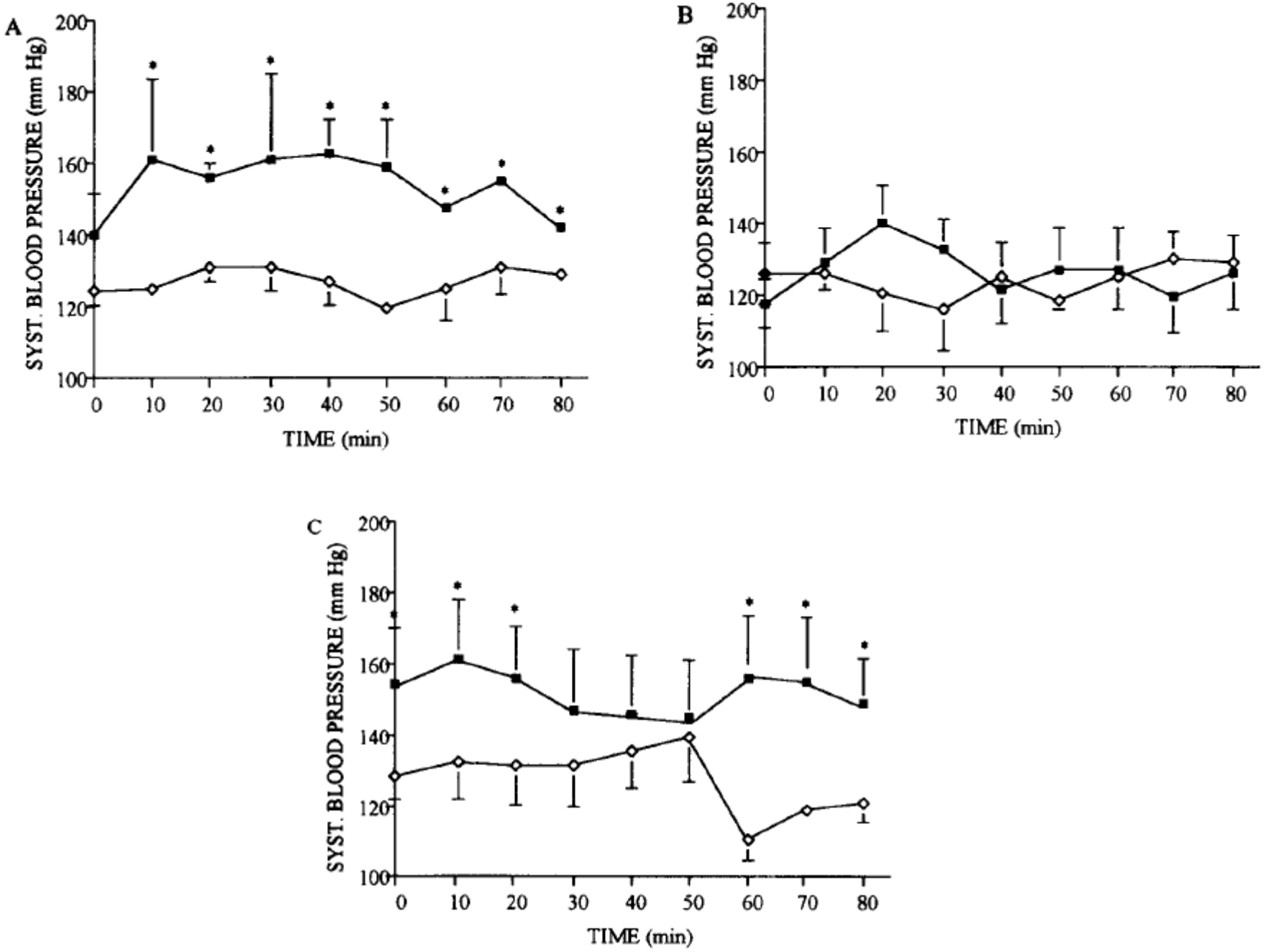
PII: S0306-4530(96)00014-5

HORMONAL RESPONSE TO STRESS IN BRITTLE DIABETES

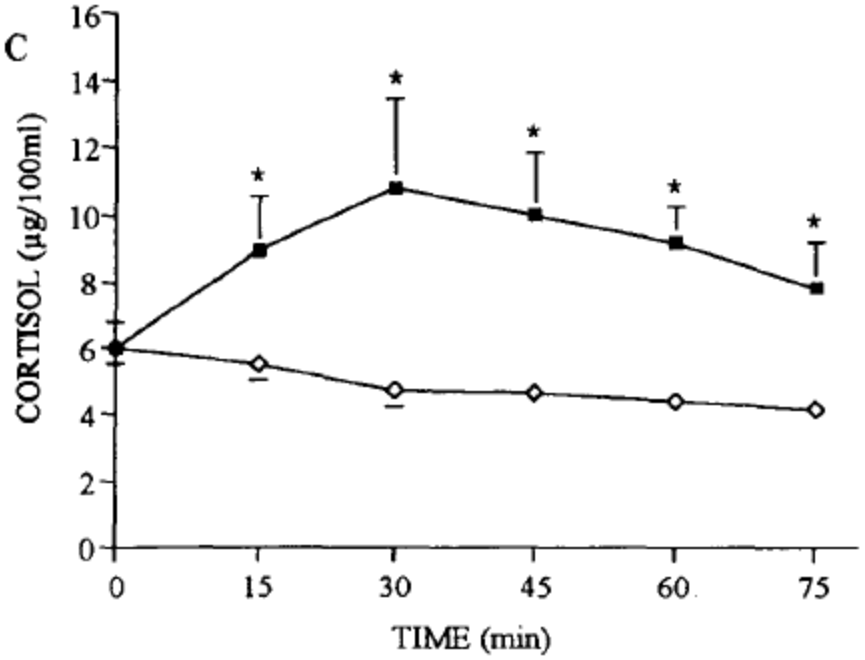
A. Dutour,[1,2] V. Boiteau,[1] F. Dadoun,[1,2] A. Feissel,[1] C. Atlan[1] and C. Oliver[1,2]

[1]Service d'Endocrinologie, Maladies Métaboliques et Nutrition, Institut Fédératif Jean Roche, Hôpital Nord, Chemin des Bourrely, 13915, Marseille Cedex 20, France; and [2]Laboratoire de Neuroendocrinolologie Expérimentale, INSERM U297, Institut Fédératif Jean Roche, Faculté de Médecine Nord, Bd Pierre Dramard, 13916, Marseille Cedex 20, France


C
HEART RATE (bpm)
180
160
140
120
100
80
60
0
10
20
30
40
50
60
70
80
TIME (min)


A
SYST. BLOOD PRESSURE (mm Hg)
200
180
160
140
120
100
0
10
20
30
40
50
60
70
80
TIME (min)
B
SYST. BLOOD PRESSURE (mm Hg)
200
180
160
140
120
100
0
10
20
30
40
50
60
70
80
TIME (min)
C
SYST. BLOOD PRESSURE (mm Hg)
200
180
160
140
120
100
0
10
20
30
40
50
60
70
80
TIME (min)

	ACTH pg/ml/min Control	Stable	Unstable
Without stress	1540 ± 315	1475 ± 246	1212 ± 83
With stress	1590 ± 177	1550 ± 263	2213 ± 439
p			$p < .05$



	Unstable
Without stress	357 ± 32
With stress	665 ± 114
p	$p < .01$

	Unstable
Without stress	705 ± 50
With stress	608 ± 36
p	NS

Acta Biomed 2014; Vol. 85, N. 1: 18-29

ORIGINAL ARTICLE

Brittle diabetes: psychopathological aspects

Lorenzo Pelizza[1], *Federica Bonazzi*[2], *Sara Scaltriti*[3], *Bruna Milli*[3], *Chierici Giuseppina*[3]

[1]CSM Guastalla, Reggio Emilia Mental Health Department; [2]Gonzaga Medical Center; [3]Diabetes Treatment Unit, Guastalla Civil Hospital, Reggio Emilia Health-Care Department, Guastalla, Italy

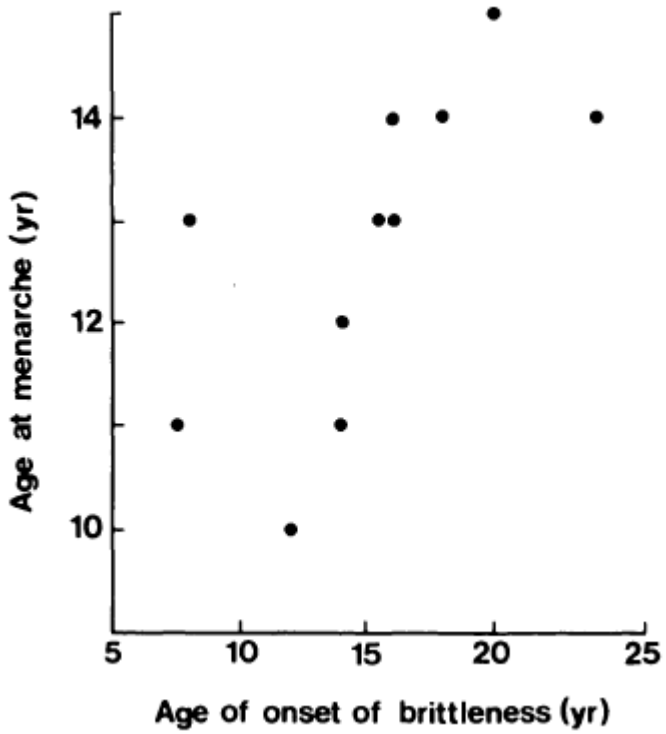
tients presented lower scores in MCMI-III compulsive personality traits and higher scores in paranoid, schizoid, schizotypal, antisocial, borderline, narcissistic, avoidant, dependent, depressive, and passive-aggressive personality traits. *Conclusions.* In this study, brittle diabetics show no differencies in terms of global severity of psychopathological distress and axis I specific DSM-IV-TR diagnoses in comparison with non-brittle subjects (except for phobic anxiety). Differently, brittle diabetics are characterized from less functional and maladaptive personality features and suffer more frequently and intensively from specific pathological personality traits of all DSM-IV-TR clusters. (www.actabiomedica.it)

Clinical Features of Brittle Diabetic Patients Unresponsive to Optimized Subcutaneous Insulin Therapy (Continuous Subcutaneous Insulin Infusion)

JOHN PICKUP, GARETH WILLIAMS, PATRICIA JOHNS, AND HARRY KEEN

DIABETES CARE, VOL. 6 NO. 3, MAY-JUNE 1983

- 14 CSII ile tdv edilen kadın hasta
- 2 grup: 12 hasta hiper, 2 hasta hipo
- 1. Grup menarşla beraber oynamalar başlamış, oligohipomenore, kilolu
- 2. Grup adetler düzenli, kırılganlığın menarşla ilgisi yok


Age at menarche (yr)
14
12
10
5
10
15
20
25
Age of onset of brittleness (yr)

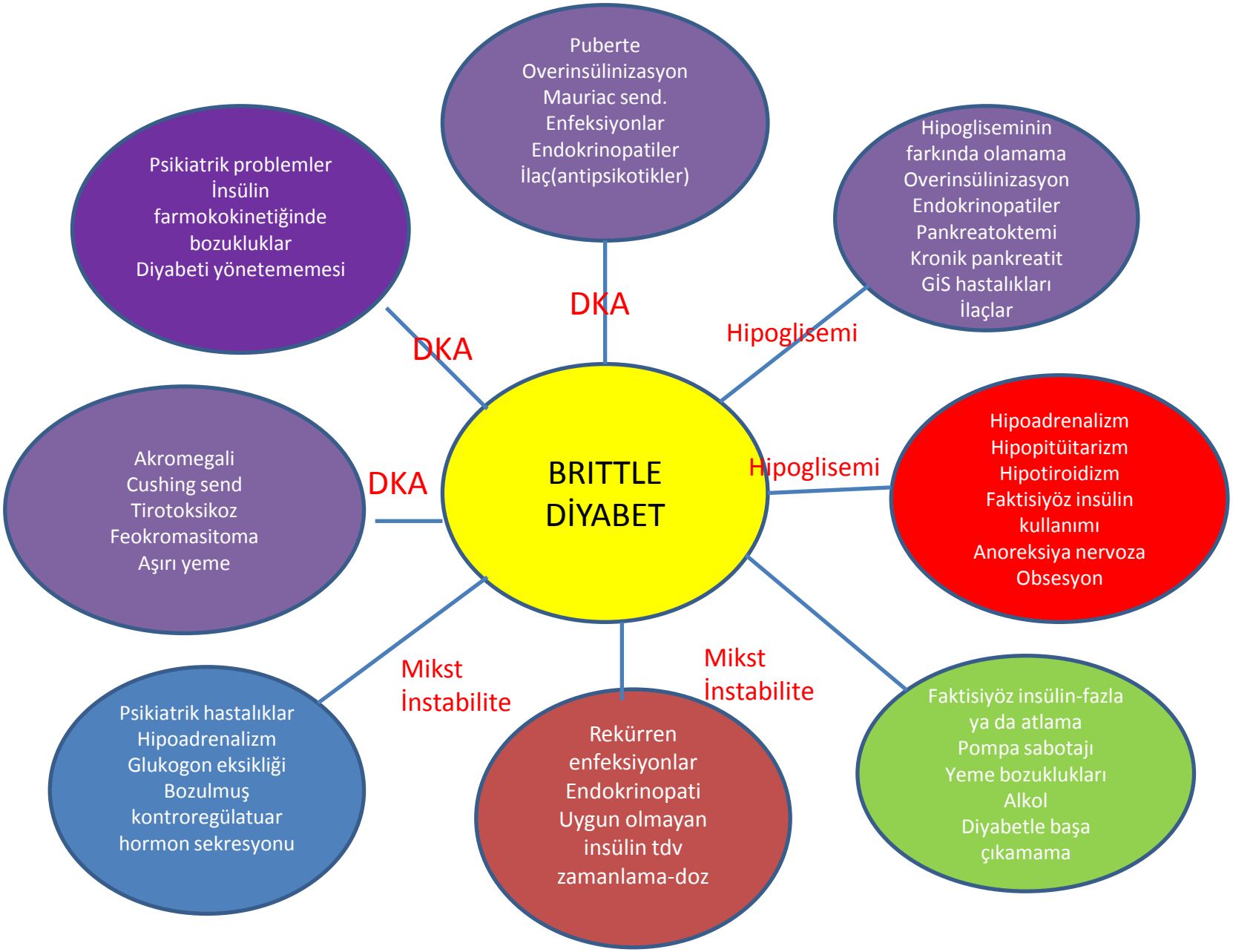
CSII

- DCTT ve birçok çalışmanın gösterdiği gibi pompa tdvsi daha iyi glisemik kontrol sağlar. Çoklu enjeksiyonlara göre A1c'de % 0.2-0.4 iyileşme ama daha da önemlisi hipoglisemi sıklığında azalma sağlar

Haakens K, et al. CSII, MI and conventional insulin therapy (CT) in self-selecting insulin-dependent diabetic patients. J Intern Med 1990 ; 228 : 457-64.

ITT endikasyonları

- Hipoglisemik farkındasızlık
- Aşırı oynaklık
- Gastroparezi
- Pompa tdv başarısızlık



Christina Voulgari et al. Diabetes technology & therapeutics. 2012

Vaka Z.D

- 57 yaş, kadın hasta,hiperglisemi ve ketonüri nedeniyle servise yatırıldı. 20 yıldır DM
- OAD alırken son 10 yılda insülin kullanıyor
- Son 6 aydır hergün 1-4 kez tekrarlayan hipoglisemi ataklarından yakınıyor

FM-ZD

- TA: 140/90 mmHg, nabız 78/dak
- Boy 145 cm., ağırlık 64 kg, VKİ: 30.4
- Ortostatik hipotansiyon tesbit edilmedi.
- Boyun muayenesinde 1 cm. çapında tiroid nodülü
- Akciğer muayenesinde ekspiryum uzaması ve sibilan ronküsler saptandı.
- KC midklaviküler hatta kosta yayını 1 cm geçiyordu.
- Yüzeyel ağrı ve dokunma duyuları her iki alt ekstremitede azalmıştı.
- Asil tendon refleksleri her iki. tarafta hipoaktifti

LAB-ZD

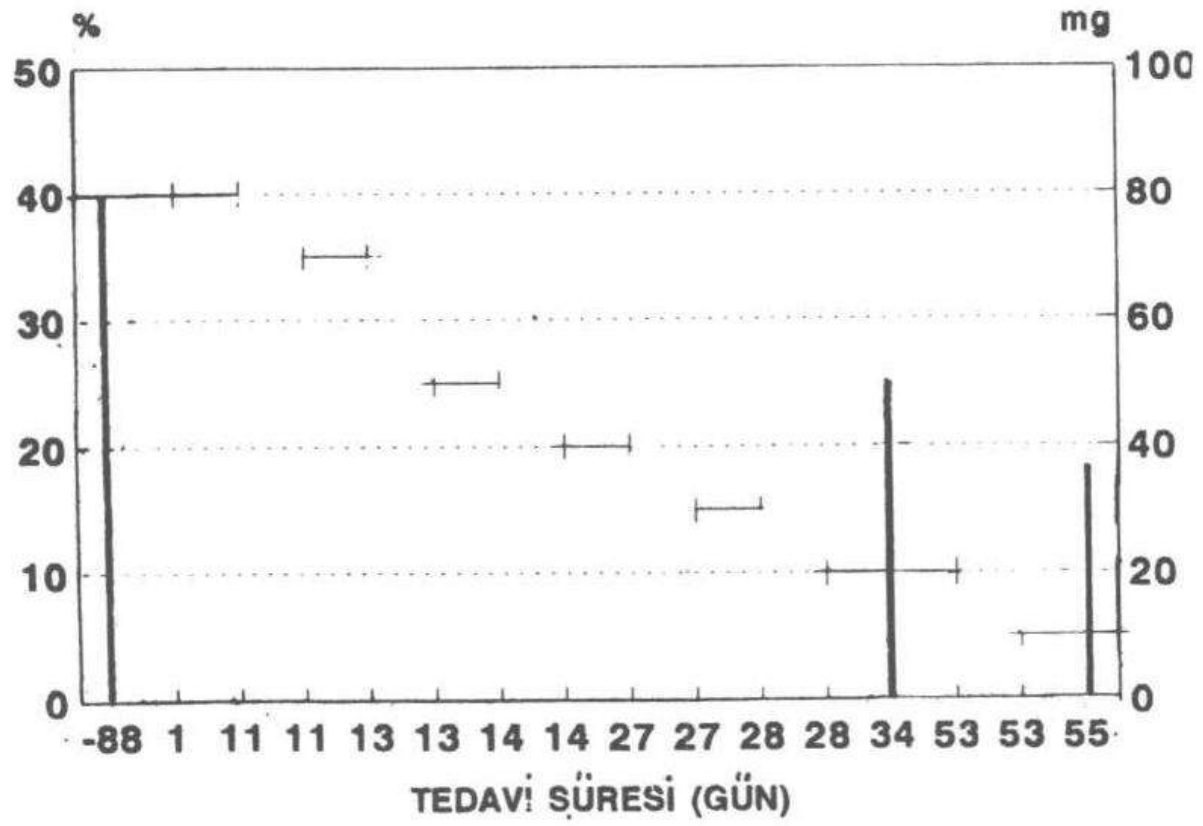
- KŞ: 275 mg/dl,
- Eş zamanlı plazma insülin seviyesi 150.1 /uU/'ml (normal : 4-25) ve plazma C-peptid 0.14 ng/ml (normal 0.8-4)
- A1c: %14.2

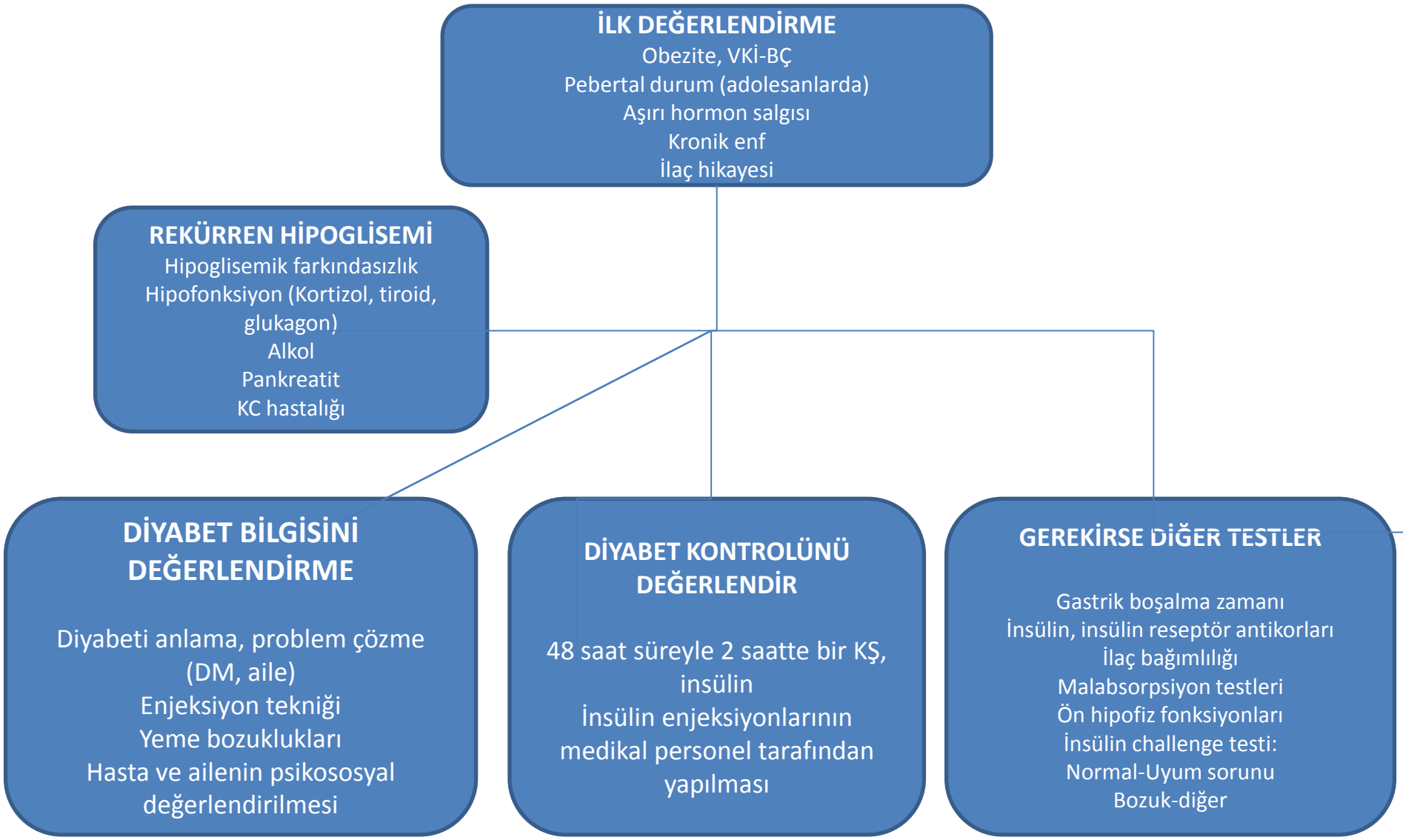
İnsülin antikoru % 40 (normal 4-10)

ANKARA TIP MECMUASI (THE JOURNAL OF THE FACULTY OF MEDICINE) Vol. 47 : 135-142, 1994

İNSÜLİN OTOANTİKORLARINA BAĞLI BİR «BRİTTLE» DİABETES MELLİTUS OLGUSU

Ali Rıza Uysal* Vedia Cesur** Gürbüz Erdoğan***





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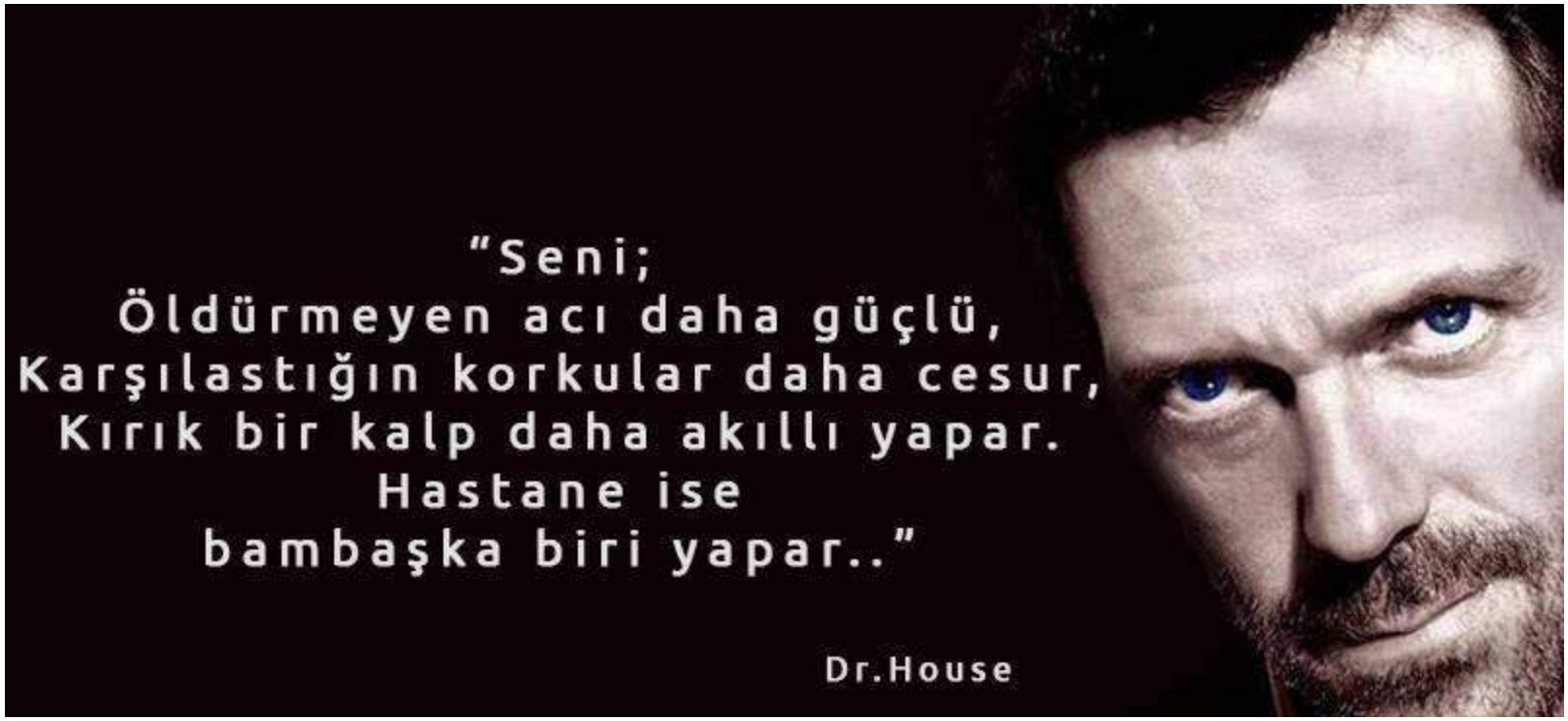

TEŞEKKÜRLER