Diabetes: Looking beyond traditional retinopathy
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Diabetes in the United States 2011*

Total: 25.8 million people (8.3%)
Diagnosed: 18.8 million people
Pre-diabetes: 70 million people
30% of people in the US are expected to have DM by 2030

Cost of DM care 2011 report
$174 billion: Total costs of diagnosed diabetes in the United States in 2007
$116 billion for direct medical costs
$58 billion for indirect costs (disability, work loss, premature mortality)
After adjustment the average medical expenditures among people with diagnosed diabetes were 2.5 times higher than what expenditures would be in the absence of diabetes.

Diabetes in the United States 2011
Incidence of DM has paralleled obesity in the US since 1994
Greatest for individuals with BMI over 30

Body Mass Index (BMI)
-calculated from a person's weight and height
-a reliable indicator of body fat
-used to screen for weight categories that may lead to health problems
-Adult (>20 yo) and youth (<20yo) calculators are used

Is obesity the cause of diabetes?

BMI calculation table for adults
So if obesity is a major player in DM development:

Can we change the eventual outcome of having diabetes by modifying our lives?

To what degree do we participate in the disease prevention education with patients?

Is diabetes preventable?

Eating a Mediterranean diet cuts risk of DM by 83%.

Moderate physical activity cuts risk of elevated BS.

Diabetes Prevention Plan (DPP)*

NIH study to determine if diabetes can be prevented in a pre-diabetic group of pts by:

- combination of lifestyle changes (ie: weight loss, physical activity and a calorie restricted diet)
- tx with metformin alone

Pre-diabetes criteria for DPP*:

- Age >18 years
- BMI >24 kg/m² (>22 kg/m² among Asian Americans)
- IGT of 2h plasma glucose 140~199 mg/dl (based on 75-g OGTT if available)
- Elevated FPG (95~125 mg/dl*)
- HDL-triglyceride ratio > 3.5

3234 patients were assigned to 1 of 3 groups:

1) lifestyle changes (to include): loss of 7% body weight, 150 minutes a week of exercise, less fat and fewer calories
2) 850mg bid of metformin
3) no intervention

Results of DPP

Lifestyle changes group:
- 58% risk reduction in all age groups
- 73% reduced risk in the over 60 age group

Metformin treated group:
- 31% risk reduction

Annual conversion to DM:
- 7.8% lifestyle change group
- 7.8% metformin
- 11% control group

So is diabetes preventable?

The DPP data supports interventions, in pre-diabetic patients, including lifestyle changes and medication do effect the onset of DM in a positive way.

Diabetes surgery?

NEJM March 26, 2012 reported on the success of BS control and weight loss in 2 surgical groups of morbidly obese DM patients. There were 150 Type 2 patients randomized into 3 groups.
Diabetes surgery to treat Type 2 DM?

150 morbidly obese patients randomized into 3 groups:
- Metformin
- Gastric banding
- Gastric bypass

GMA March 27, 2012: Dr. Nancy Snyderman:
...if you think about the kind of budget conversations we have in this country or Germany, bailing out Greece, there isn't enough money in the bank to take care of this epidemic... if you look at the global toll, it is estimated that by 2030, 10% of people worldwide will be diabetic....

Cost of surgery between $15K and $20K p/p

Insurance companies may opt to cover the surgery as viable intervention.

Diabetic retinopathy:
What we know from DR studies

The DCCT (1100M) and UKPDS (1300M) demonstrated the benefits of tighter control decreased the incidence and progression in microvascular disease.

Metabolic memory improved with intensive treatment early after the diagnosis thereby decreasing the severity of long-term complications.

ACCORD Study 2010
Action to Control Cardiovascular Risk in Diabetes

Can intensive treatment decrease a major vascular event?
- BS (A1C of 6 range vs 7-7.9 range)
- BP (normal levels vs conventional levels)
- Hb (fibrate and statin drug)

- 22% increased risk of death from tight BS control group
- 40% less risk of death in tighter BP group
- Hb treatment safe but no decreased risk of CV/AI or death

Veterans Affairs Diabetes Trial 2009

Reducing proteinuria. BS control vs no control

- 22% reduced CV event and death by 40%
- No real benefit
- 38% less risk of CV event vs death by 200%
Tight control is not for every diabetic patient!
Educate your patient with caution!

Diabetic neuropathy and the eye
• Optic neuropathy
  Diabetic papillopathy
  AION
• CN palsy
  III
  IV
  VI

Microvascular CN palsies
• Isolated CN III, IV or VI
• Ischemic event in the brainstem/subarachnoid space or possibly in cavernous sinus
• 20% of microvascular CN III have pupil enlargement so compressive etiology must be ruled out

OS CN III palsy
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OS CN IV palsy

OS CN VI palsy
Most common DM associated microvascular CN palsies

CN palsy work-up
BP
Blood work: serum glucose/CBC/SED rate lipid profile
Imaging: immediate vs delayed?
Diabetic papillopathy

- 1965 Freund reported 2 cases of papilledema and papillitis in diabetes.
- 1971 Lubow reported on pseudopapilledema and diabetes.
- 1980 Appen RE et al reported 2 cases of disc edema in patients with juvenile diabetes mellitus.
- 1981 Hayreh reported 3 cases of acute optic neuropathy in juvenile diabetes mellitus.

Diabetic papillopathy etiology

- 1965 Freund attributed it to AION.
- 1971 Lubow attributed it to AION.
- 1980 Appen et al attributed it to diabetic vasculopathy and not AION.
- 1981 Hayreh felt this DID represent an AION variant despite the young age of the patient.

Examples of disc ischemia etiology*

- YOUNG
  - Collagen vascular disease
  - Hematologic disorders
  - Cardiac
  - Eclampsia

- ADULT
  - Atherosclerosis
  - Arteriosclerosis
  - Hypertension

Hayreh SS. Zahoruk RM; Anterior ischemic optic neuropathy: VI. In juvenile diabetics. Ophthalmologica 1981; 182:13-28

Similarities of AION/diabetic papillopathy

- Ischemia not an "all or none" phenomenon.
- Diabetic microangiopathy and rheologic factors (ie: hypercoagulability, decreased RBC distensibility) contribute to variable levels of ischemia to disc.

Similarities of AION/diabetic papillopathy

- AION in young diabetes with relatively good VA.
- Predominantly unilateral but can be bilateral.
- Retinopathy present in 80% of reported cases.
- Vitreal traction on nerve implicated.

1) Disc related VF defects
2) Dilated/telangiectatic vessels on the disc surface
3) Bilateral involvement possible
4) Subsequent optic atrophy
5) Segmental filling of short posterior ciliary vessels
6) Variable but predominantly significant visual recovery.


Other implications of diabetic papillopathy

- Sometimes associated with macular edema.
- Reported in patients with crows feet and rapid glycemic control.
- A 1.5 drop in HbA1c in 1 year.
- No specific treatment case reports show improvement in subtenon/intravitreal bevacizumab, as well as Arsenic.*

Diabetic papillopathy patient characteristics

- Regillo et al reported 27 eyes of 20 patients.
- 25% of pts had Type 2 DM with average age of 97.
- Disc involvement for 5.3 yrs.
- 78% had macular edema.
- 15% had visual acuity worse than 20/50.

Other considerations of DP

- Prognostic indicator for progressive PDR.
- Higher incidence of:
  - Hypertension
  - Ischemic heart disease
  - TIAs
  - Second eye involvement.
  - Surface telangiectatic vessels usually.
Take home on AION/diabetic papillopathy
1) Disc edema usually resolves in about 2 mos
2) Prominent surface vessels can mimic NVD
3) Diabetic disc edema not always benign entity as some patients have permanent/ significant visual loss
4) Awareness may prevent unnecessary laser PRP

Diabetes and Glaucoma Risk: Real?
GRET: proposed DM as a positive/protective systemic factor with linked to the development of glaucoma.

DM and Glaucoma
- Distinctive blood flow abnormalities in glaucoma patients with diabetes reported March 2012:
  - peak systolic velocity of the CRA was 17% lower
  - corresponding decrease in:
    - ocular perfusing pressure
    - temporal posterior ciliary artery resistance
    - nasal posterior ciliary artery resistance
  - average RNFL thin correlated with the decrease flow in CRA and posterior ciliary arteries
  - larger avascular/non flow areas at the superior and inferior areas of the ONH


There was no negative correlations in the non-diabetic OAG patients!
There is a negative correlation for the diabetic OAG patients.

DM and Glaucoma
The is a negative correlation for the diabetic OAG patients.

Moderate HT resolved with treatment
BP140/95
H r/o past Tis
BP135/84

Shared retinal findings with DM
- hemorrhage (dot and flame) and microaneurysms
- microinfarcts
- exudates
- high risk of clinical strokes
- death from coronary heart disease


What about BP control in Diabetics?
- Poor HT control over 140/90 contributes to progressive diabetic retinopathy
- Ts with Enalapril and Losartan reduced the incidence and progression of HT by 65% and 70% respectively in non-diabetic Type 1 DM patients*

Decreased prominence of MAs and heme with BP control

Target BP levels for pts with DM is 130/85 or less so consider HT as complicating factor for progressive diabetic retinopathy even if classic HR is not present

Normotensive BP levels can be associated with morbidity

Some things to remember about HR!

Anemia and diabetic retinopathy

Mikajira and Nishikawa* reported 2 cases of diabetic retinopathy with combined diabetes and anemia.

Both cases had reversible retinopathy with treatment of the anemia.

Anemic considerations for diabetic retinopathy

Shorb reported 3 cases of rapid progression to PDR with the onset of severe anemia.

Berman and Friedman reported 3 cases of resolution of retinal exudation with treatment of anemia.

ETDRS and risk factors for diabetic retinopathy

Identified 4 additional risk factors for retinopathy: neuropathy, low hematocrit, increased triglyceride and decreased albumin.

A 2x risk for progression to PDR in anemic patients

Anemia breakdown

1/3 of cases malnutrition/malabsorption

1/3 cases chronic kidney disease

(ie: diabetic nephropathy...)

1/3 other conditions

World Health Organization

Hemoglobin threshold used to define anemia

<table>
<thead>
<tr>
<th>Age or gender group</th>
<th>Hemoglobin threshold (g/dl)</th>
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<tbody>
<tr>
<td>Children 5-15</td>
<td>12</td>
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<tr>
<td>Children 15-18</td>
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<tr>
<td>Women (non pregnant)</td>
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<tr>
<td>Women (pregnant)</td>
<td>11</td>
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<tr>
<td>Men</td>
<td>13</td>
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Case 1
Case 2

In Summary

Diabetes is possibly preventable

Tighter control of BS is beneficial to delay onset and slow down progression of microvascular disease even after 20 yrs.

Systemic control paramount to retinopathy control!

Tight BS control may be beneficial for most people but can be fatal for others. Remember increased risk of CV event and death by 200% > 20yrs DM.