Diabetic Retinopathy
Overview

- This presentation covers the following topics:
  - Definitions
  - Epidemiology of diabetic retinopathy
  - Evidence for public health approaches
  - Screening for diabetic retinopathy
  - Health education

Notes section – a more detailed explanation is provided in the notes along with key references.
WHO definition DM (2006)

• Chronic disease, which occurs when the pancreas does not produce enough insulin, or when the body cannot effectively use the insulin it produces.

• Primarily defined by the level of hyperglycaemia giving rise to risk of microvascular damage (retinopathy, nephropathy, and neuropathy).

• Diagnostic criteria:
  fasting plasma glucose ≥ 7.0 mmol/l (126mg/dL)
  or
  2–h plasma glucose ≥ 11.1 mmol/l (200mg/dL).
Magnitude of Diabetes Mellitus

- Globally 2005 > than 170 million DM patients
- Global estimates 2010: 285 million DM patients
Prevalence of diabetes

The top 10 countries, in numbers of people with diabetes, are:

India
China
USA
Indonesia
Japan
Pakistan
Russia
Brazil
Italy
Bangladesh

<table>
<thead>
<tr>
<th>Year</th>
<th>Ranking</th>
<th>Country</th>
<th>People with diabetes (millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>1</td>
<td>India</td>
<td>31.7</td>
</tr>
<tr>
<td>2000</td>
<td>2</td>
<td>China</td>
<td>20.8</td>
</tr>
<tr>
<td>2000</td>
<td>3</td>
<td>United States of America</td>
<td>17.7</td>
</tr>
<tr>
<td>2030</td>
<td>1</td>
<td>India</td>
<td>79.4</td>
</tr>
<tr>
<td>2030</td>
<td>2</td>
<td>China</td>
<td>42.3</td>
</tr>
<tr>
<td>2030</td>
<td>3</td>
<td>United States of America</td>
<td>30.3</td>
</tr>
</tbody>
</table>

Source: Wild et al. 2004

Prevalence of diabetes (%) in persons 35 - 64 years

< 3  3 - 5  6 - 8  > 8

2000 = number of people with diabetes in 2000
2030 = number of people with diabetes in 2030
Trends in DM epidemiology

Why the increase?
- Population growth
- Population aging
- Urbanization
- Lifestyle change
- Obesity

Trend
- Most rapid changes in low and middle income countries

DM and blindness: After 15 years of DM estimated:
- 2% become blind
- 10% develop severe visual impairment.
I might suggest longer lifespans for diabetics because it is duration of diabetes that is key here
Marissa Carter, 6/2/2011

This slide is epi for DM, I think you are refering to DR epi in the comment
Covadonga Bascaran, 7/11/2011
Definition and classification of DR

• Characteristic group of lesions found in the retina of individuals that have had diabetes for several years.

• It is considered to be the result of vascular changes in the retinal circulation: a microangiopathy that exhibits features of both microvascular occlusion and leakage.
International classification

- **R0 None**
  - No retinopathy

- **R1 Mild**
  - Microaneurysms only

- **R2 Moderate**
  - More than microaneurysms but not severe

- **R3 Severe**
  - More than 20 haemorrhages
  - Venous beading
  - IRMA

- **R4 Proliferative**
  - New vessels
  - Vitreous haemorrhage

- **M0 No maculopathy**
  - No macular oedema

- **M1 Mild maculopathy**
  - Exudate / oedema away from fovea

- **M2 Moderate maculopathy**
  - Exudate / oedema close to fovea

- **M3 Severe maculopathy**
  - Exudates / oedema at fovea
discuss this slide.
ICRUDPAT, 3/22/2011
Covadonga Bascaran, 7/11/2011
Prevalence DR USA (WESDR)

- Prevalence of DR of **any severity** in the diabetic population as a whole is approximately **30%**.
- Prevalence DR with **risk of visual impairment** is approximately **10%**.

<table>
<thead>
<tr>
<th>Duration</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1 IDDM</td>
<td></td>
</tr>
<tr>
<td>&lt;5 yrs</td>
<td>13%</td>
</tr>
<tr>
<td>10-15 yrs</td>
<td>90%</td>
</tr>
<tr>
<td>Type 2 IDDM</td>
<td></td>
</tr>
<tr>
<td>&lt;5 yrs</td>
<td>40%</td>
</tr>
<tr>
<td>15-20 yrs</td>
<td>84%</td>
</tr>
<tr>
<td>Type 2 NIDDM</td>
<td></td>
</tr>
<tr>
<td>&lt;5 yrs</td>
<td>24%</td>
</tr>
<tr>
<td>15-20 yrs</td>
<td>53%</td>
</tr>
</tbody>
</table>
I find the prevalence data interesting for type 2 between IDDM and NIDDM groups; is that a general finding for other studies?

Marissa Carter, 6/2/2011
What do we know about the epidemiology of DR

• Mainly based on population-based studies from developed countries.

• Difficulties in comparing data due to varied study methodologies:
  ➢ Population-based/hospital-based or varied by DM type
  ➢ Varied age of inclusion, duration/onset of DM
  ➢ Sample size
  ➢ Definitions and classification.
# Examples of DR prevalence surveys

<table>
<thead>
<tr>
<th>Country</th>
<th>Sample</th>
<th>Age</th>
<th>Prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA WESDR (1)</td>
<td>996</td>
<td>&lt;30</td>
<td>19.0</td>
</tr>
<tr>
<td></td>
<td>1370</td>
<td>&gt;30</td>
<td>28.8</td>
</tr>
<tr>
<td>USA LALES (2)</td>
<td>1217</td>
<td>&gt;40</td>
<td>46.9</td>
</tr>
<tr>
<td>India-Chennai CURES (3)</td>
<td>1382</td>
<td>&gt;20</td>
<td>17.6</td>
</tr>
<tr>
<td>UK Liverpool</td>
<td>395</td>
<td>15-92</td>
<td>33.0</td>
</tr>
<tr>
<td>Barbados (5)</td>
<td>636</td>
<td>&gt;40</td>
<td>28.5</td>
</tr>
<tr>
<td>Australia Blue Mountains (6)</td>
<td>255</td>
<td>&gt;50</td>
<td>32.0</td>
</tr>
<tr>
<td>China Beijing (7)</td>
<td>235</td>
<td>&gt;40</td>
<td>37%</td>
</tr>
</tbody>
</table>
Diabetic retinopathy and blindness

• Leading cause of blindness in working age population

• Globally estimated prevalence of blindness due to DR 5% (1.8 million persons) in 2002:
  - 0% (unknown) Africa
  - 3–7% South-East Asia and Western Pacific
  - 15–17% Europe, USA Europe
## Risk factors for DR

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Modifiable/non modifiable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration</td>
<td>No</td>
</tr>
<tr>
<td>Poor glycaemic control</td>
<td>YES</td>
</tr>
<tr>
<td>Hypertension</td>
<td>YES</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>PARTLY YES</td>
</tr>
<tr>
<td>Puberty</td>
<td>NO</td>
</tr>
<tr>
<td>Renal disease</td>
<td>PARTLY YES</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>YES</td>
</tr>
</tbody>
</table>
I agree but there is a risk of increased hypoglycemic episodes and death if control is too tight

Marissa Carter, 6/2/2011
WESDR: Cumulative 10-yr Incidence

**VISUAL IMPAIRMENT**
- 9.4% in young IDDM
- 37.2% in older IDDM
- 23.9% in older NIDDM

**BLINDNESS**
- 1.8% young IDDM
- 4.0% older IDDM
- 4.8% older NIDDM

Factors influencing incidence:
- Baseline retinopathy at diagnosis
- Glycaemic management – insulin
- Poor DM control – high HbA1c
- Duration
Management of DR

- Laser – first line treatment for DR
- Vitrectomy
- Experimental treatments
  - Anti-VEGF
  - Intra-vitreal steroid
# Management of DR

<table>
<thead>
<tr>
<th>Stage of Disease</th>
<th>Management options</th>
</tr>
</thead>
<tbody>
<tr>
<td>No DR or moderate non-proliferative DR</td>
<td>Optimize medical glycaemic control, blood pressure and lipids</td>
</tr>
<tr>
<td>Severe non-proliferative DR</td>
<td>Consider scatter (pan-retinal) laser photocoagulation. Better visual prognosis</td>
</tr>
<tr>
<td>Proliferative DR</td>
<td>Immediate pan-retinal photocoagulation. Additional vitrectomy for high-risk cases</td>
</tr>
<tr>
<td>High risk PDR not amenable to laser treatment</td>
<td>Vitrectomy</td>
</tr>
<tr>
<td>CSME (clinically significant macular edema)</td>
<td>Focal and or pan-retinal photocoagulation</td>
</tr>
</tbody>
</table>
# Evidence for treatment of DR

<table>
<thead>
<tr>
<th>Trial</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diabetic Retinopathy Study (DRS)</strong></td>
<td>PRP reduces the risk of severe visual loss by &gt; 50% in high-risk proliferative diabetic retinopathy</td>
</tr>
</tbody>
</table>
| **Early Treatment Diabetic Retinopathy Study (ETDRS)** | 1. Focal photocoagulation treatment for macular oedema.  
2. No scatter treatment for eyes with mild to moderate NPDR, unless high risk.  
3. Early vitrectomy for advanced active PDR.  
4. Careful follow-up for all DR patients.  
5. No ocular contraindications for aspirin |
| **Diabetic Retinopathy Vitrectomy Study (DRVS)** | 1. Early vitrectomy in eyes with recent severe vitreous hemorrhage especially if IDDM.  
2. Early vitrectomy in very severe PDR                                                                                                       |
## Evidence for prevention

<table>
<thead>
<tr>
<th>Trial</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>United Kingdom Prospective Diabetes Study (UKPDS)</td>
<td>Lowering elevated blood glucose and BP levels significantly reduces life-threatening complications of type 2 diabetes</td>
</tr>
<tr>
<td>Diabetes Control and Complications Trial (DCCT)</td>
<td>Intensive treatment reduces risk of ocular disease (76%), renal disease, and neuropathy</td>
</tr>
</tbody>
</table>
Public health approach – to prevent visual loss due to DM

• **Primary (to stop the DR from occurring)**
  - Health education, dietary/lifestyle changes
  - Early diagnosis of diabetes
  - Control of hyperglycaemia, hypertension, and dyslipidemia

• **Secondary (to prevent blindness from occurring)**
  - Controlling hyperglycemia, hypertension, and dyslipidemia
  - Screening to detect treatable retinopathy
  - Provision of laser photocoagulation

• **Tertiary (to treat the blinding disease)**
  - Vitreo–retinal surgery

Rehabilitation of VI and blind
Annual screening or merely unspecified periodic screening because of CE controversy over frequency?

Marissa Carter, 6/2/2011

Discussed in later slide in detail

Covadonga Bascaran, 7/11/2011
Screening

• Screening aims to answer simple question:

  ➢ Screening is a public health service,
  ➢ for members of a defined population,
  ➢ they may not necessarily perceive they are at risk of, or are already affected by a disease or its complications,
  ➢ are offered a test, to identify individuals who are most likely to benefit from further tests or treatment to reduce the risk of a disease or its complications
## Required criteria for screening

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Diabetic Retinopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well defined, public health problem</td>
<td>YES</td>
</tr>
<tr>
<td>Known prevalence</td>
<td>YES</td>
</tr>
<tr>
<td>Known natural history</td>
<td>YES</td>
</tr>
<tr>
<td>Simple and safe test available</td>
<td>YES</td>
</tr>
<tr>
<td>Cost-effective</td>
<td>YES</td>
</tr>
<tr>
<td>Acceptability by patients and professionals</td>
<td>YES</td>
</tr>
<tr>
<td>Agreed policy on treatment</td>
<td>YES</td>
</tr>
</tbody>
</table>
Problem is that a lot of patients don't care
Marissa Carter, 6/2/2011
Components of a screening programme

- Identification of diabetic patients
- Call/Recall mechanism
- Screening method
- Grading
- Referral network
- Treatment and follow-up pathway
- Information system
- Quality assurance
Sensitivity and specificity

• Sensitivity: the fraction of those with the disease correctly identified as positive by the test.

• Specificity: the fraction of those without the disease correctly identified as negative by the test.

• A DR screening program test must achieve 80% sensitivity and 95% specificity. (1)

• A high coverage is essential for an effective screening programme.
How do we define “high”? >= 80%
Marissa Carter, 6/2/2011

UK programme aims for a minimum of 80%, with the objective to increase coverage annually.
Covadonga Bascaran, 7/11/2011
Screening options

• **Ophthalmoscopy** by trained health personnel
  - Lower sensitivity.
  - May be the cheaper option in the initial stages

• **Retinal photography**
  - Higher sensitivity
  - Expensive
  - Permanent visual record if digital
  - Any ungradeable photos will need clinical examination using ophthalmoscopy.
## Screening Personnel

<table>
<thead>
<tr>
<th>Professional</th>
<th>Ophthalmoscopy</th>
<th>Retinal photographs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
</tr>
<tr>
<td>GP</td>
<td>25-66%</td>
<td>75-98%</td>
</tr>
<tr>
<td>Optometrists</td>
<td>48-82%</td>
<td>94%</td>
</tr>
<tr>
<td>Ophthalmol</td>
<td>43-79%</td>
<td>89-100%</td>
</tr>
<tr>
<td>Diabetologist</td>
<td>27-73%</td>
<td>98%</td>
</tr>
</tbody>
</table>
Intervals for screening

• Regular and timely to prevent blindness.

• Cost effective: systematic screening is expensive.

• Acceptability: especially as patients are asymptomatic

• Long intervals – may reduce coverage.

Liverpool diabetic eye study:
• No DR– no risk factors – 3 years.
• No DR – insulin use >20 yrs – 1 year
• Mild pre-proliferate – 4 months
• Longer intervals for patients who are low risk (70%) = cost savings
Trade off between performance and cost

• Local decisions need to be made based on:
  • Available infrastructure
  • Available resources
  • Social models for service delivery
  • Models of screening technique, will need to be country specific.

• Standardised definitions and performance measures allow for comparable measures and maintaining quality.
Models of screening

• **Static**: Based at a health/optometry center/GP practice. Must be linked to an image grading center.

• **Mobile screening**: An equipped van travels in a catchment area. Also linked to image grading center.

**Pathways:**

All photo images go to reading center for grading.

Grading and advice for referral is communicated to patient.

Ungradeable images – patients see an ophthalmologist.

Quality checks – done by ophthalmologist.
Cost effectiveness of screening for DR

• Screening is cost effective than opportunistic examinations.
• Screening annually versus every 3 years and 5 years has shown to be marginally beneficially.
• Greatest benefit for annual screening is for younger, poorly controlled diabetics.
• Most modeling done to date is based on populations on high income countries.
Acceptance and barriers of screening for DR

**Compliance challenges:**
- Asymptomatic condition
- Longer screening periods in lower risk cases:
  - might lead to poorer compliance
  - wrong message: visual loss not “my problem”
- Multiple health problems and health appointments.

**Barriers:**
- Lack of awareness about DR as cause of blindness
- Fear of laser
- Inconvenience
- No family/employers support
- Guilt about glycaemic control
- Retinal images good impact for health education
Health education for DR

• Diabetic patients should receive adequate information regarding glycaemic control, diet and exercise

• Lack of persistent behavioural change in patients despite health education – remains a challenge

• Marketing approach about the regular consultations and treatment is essential

• Orient educational messages to each culture
Conclusions on public health for DR

• DR is the leading cause of blindness in the working population and the trend is for it to increase.

• There are evidence-based strategies for the DR management and prevention of blindness.

• Screening for DR is a cost-effective tool for prevention of visual loss due to DR.

• Screening models need to be tailored for local resources.

• Health education and addressing patient barriers are essential to increase compliance with screening and treatment.