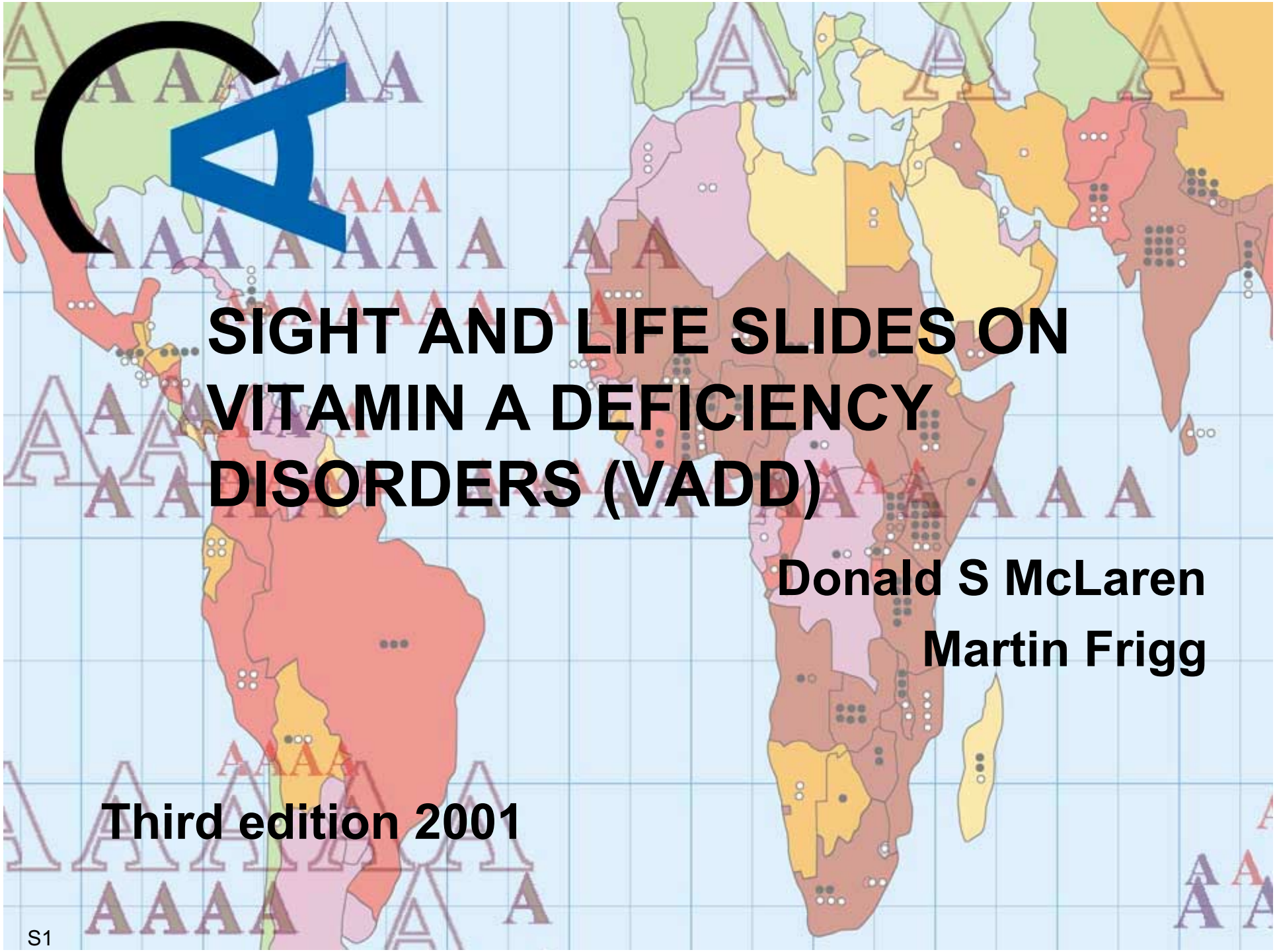


SIGHT AND LIFE SLIDES ON VITAMIN A DEFICIENCY DISORDERS (VADD)

Donald S McLaren

Martin Frigg

Third edition 2001

SIGHT AND LIFE activities

- provides vitamin A
- gives technical assistance
- supports field projects and scientific research
- gives training and education grants
- supports publications
- disseminates educational materials
- publishes a newsletter on the fight against vitamin A deficiency

Major nutritional deficiency diseases

- Protein-Energy Malnutrition (PEM)
- Vitamin A Deficiency Disorders (VADD)
- Nutritional anaemias (esp. Iron)
- Iodine Deficiency Disorders (IDD)

Vitamin A Deficiency Disorders (VADD)

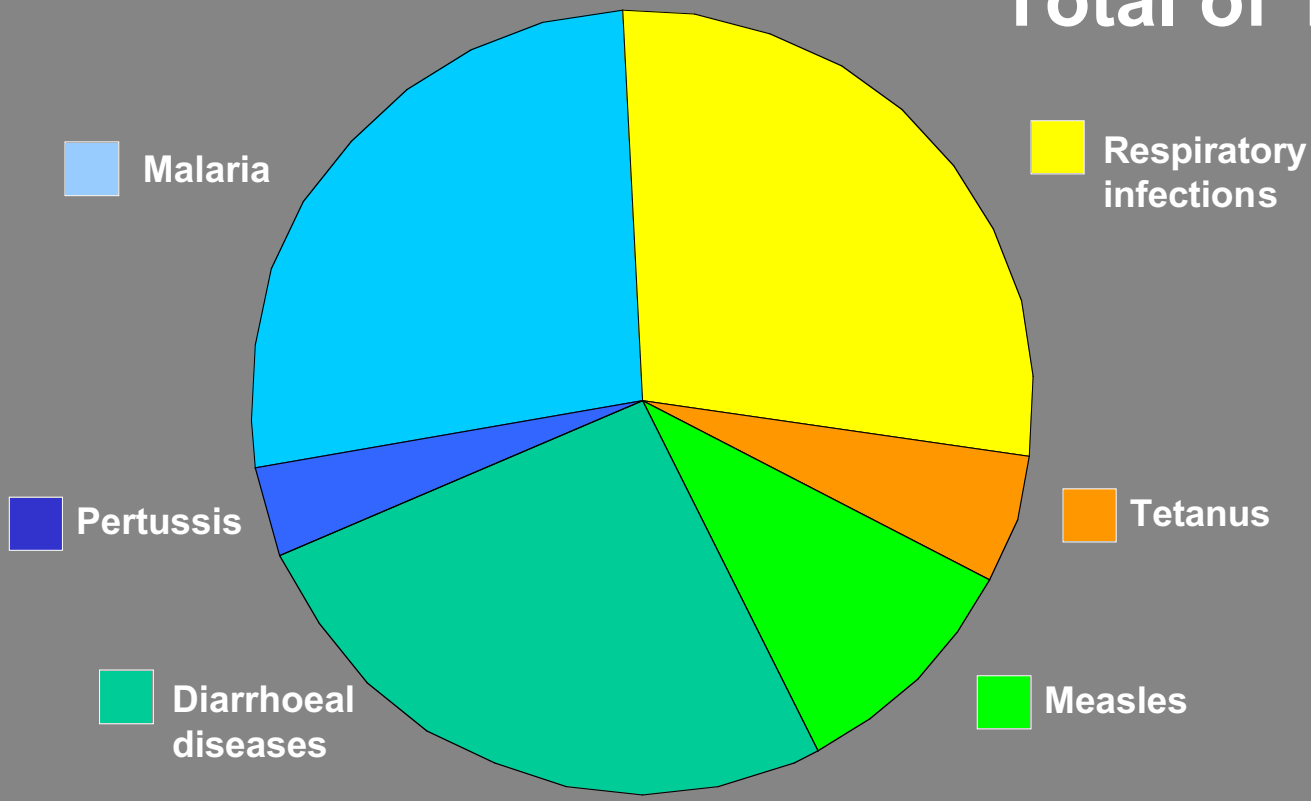
A comprehensive term that covers all effects of the deficiency state including those on health, survival and vision

Impact of VADD on public health

- **250 million pre-school-age children are subclinically vitamin A deficient**
- **3 million have clinical xerophthalmia**
- **300,000 are blind from xerophthalmia**
  (about 10% of all blind children)

Causes of child death

Total of 11.1 million



UNICEF, 1994

Impact of vitamin A intervention on child survival

”Improvement of vitamin A status in young child populations…leads to a reduction in all-cause mortality rates of about 23%”
United Nations, 1993

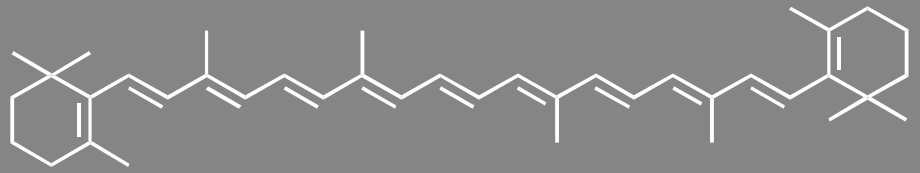
”Improved vitamin A nutriture would be expected to prevent approximately 1.3-2.5 million deaths annually among children aged under 5 years.”
Bulletin of WHO, 1992

Historical background

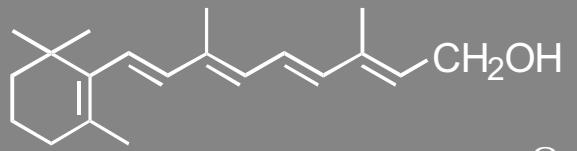
1816	Xerophthalmia in experimental animals
1904	First large human epidemic in Japan
1913	”Fat soluble A” discovered in the USA
1930	Formulae of β-carotene and vitamin A discovered (Karrer, Switzerland)
1947	Industrial vitamin A synthesis (Isler at Roche, Switzerland)
1964	First global survey of VADD
1980s	Importance of vitamin A in child survival shown

Chemistry

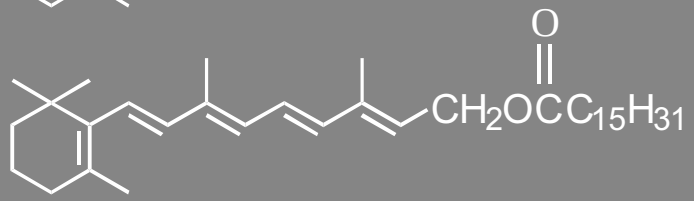
all-*trans* β-carotene



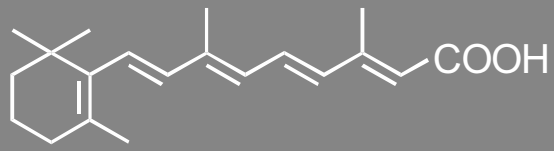
all-*trans* retinol



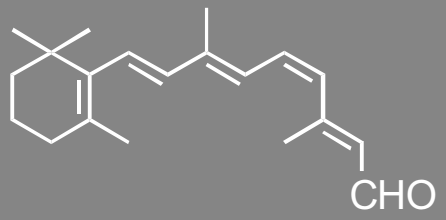
retinyl palmitate



all-*trans* retinoic acid



11-*cis* retinal



Vitamin A requirements

Retinol Equivalents (RE) per day
(1 RE = 1 µg retinol)

Child	**1-6 years**	**400 RE**
Adult	**Women**	**500 RE**
	Men	**600 RE**
Pregnancy		**600 RE**

FAO/WHO, 1983

Major food sources

- Dark green leafy vegetables
- Yellow fruits
- Carrots
- Palm oils
- Liver and liver oils

Examples of fruits and vegetables

Children being taught about foodstuffs rich in vitamin A

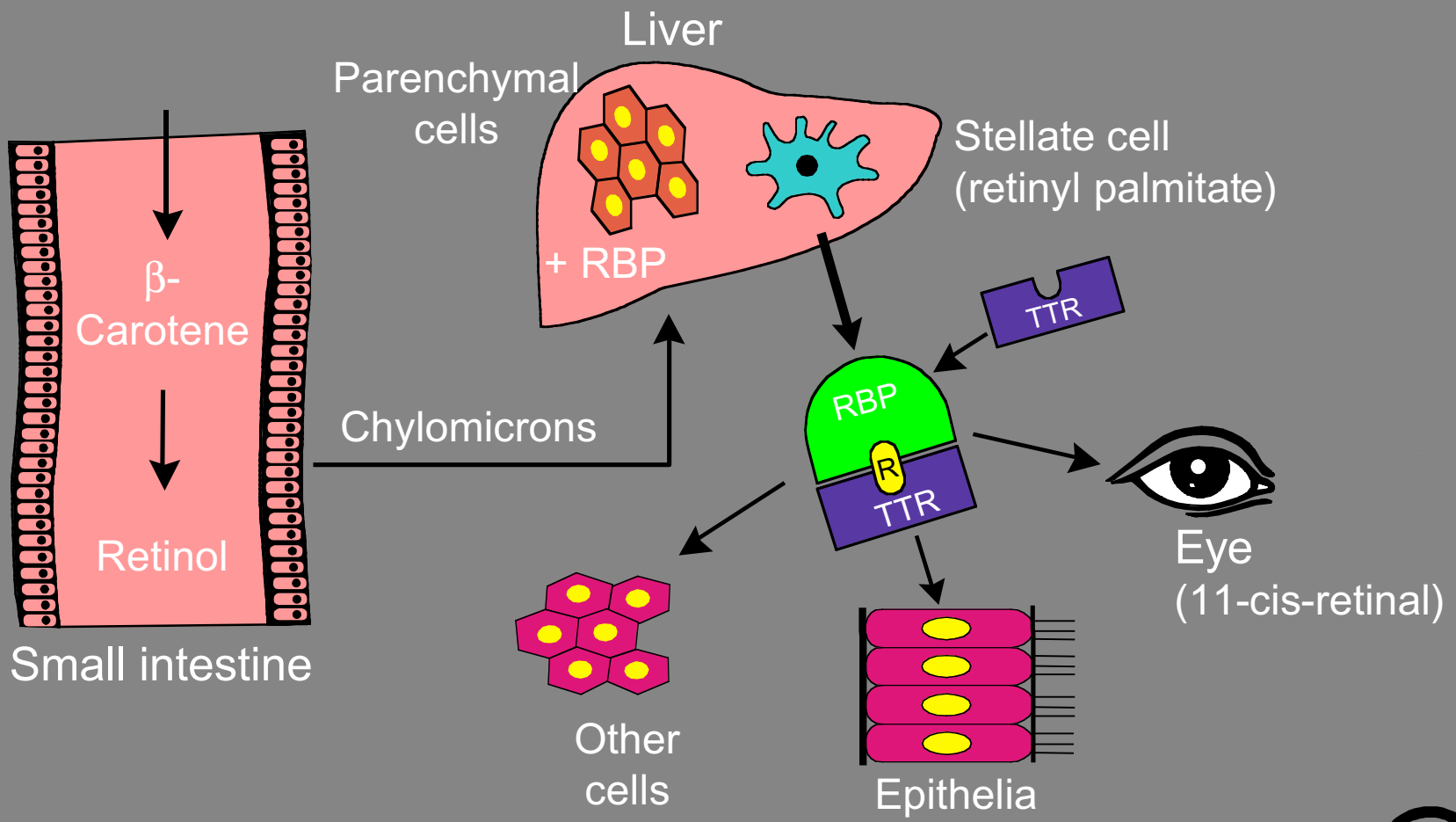
Representative values of vitamin A activity in some foodstuffs

		µg Retinol Equivalents per 100 g edible portion
Vegetable sources	mango	307
	papaya	124
	carrot	2,000
	dark green leafy vegetables	685
	red palm oil	30,000
Animal sources	butter	830
	eggs	140
	milk	40
	liver	15,000
	cod liver oil	18,000

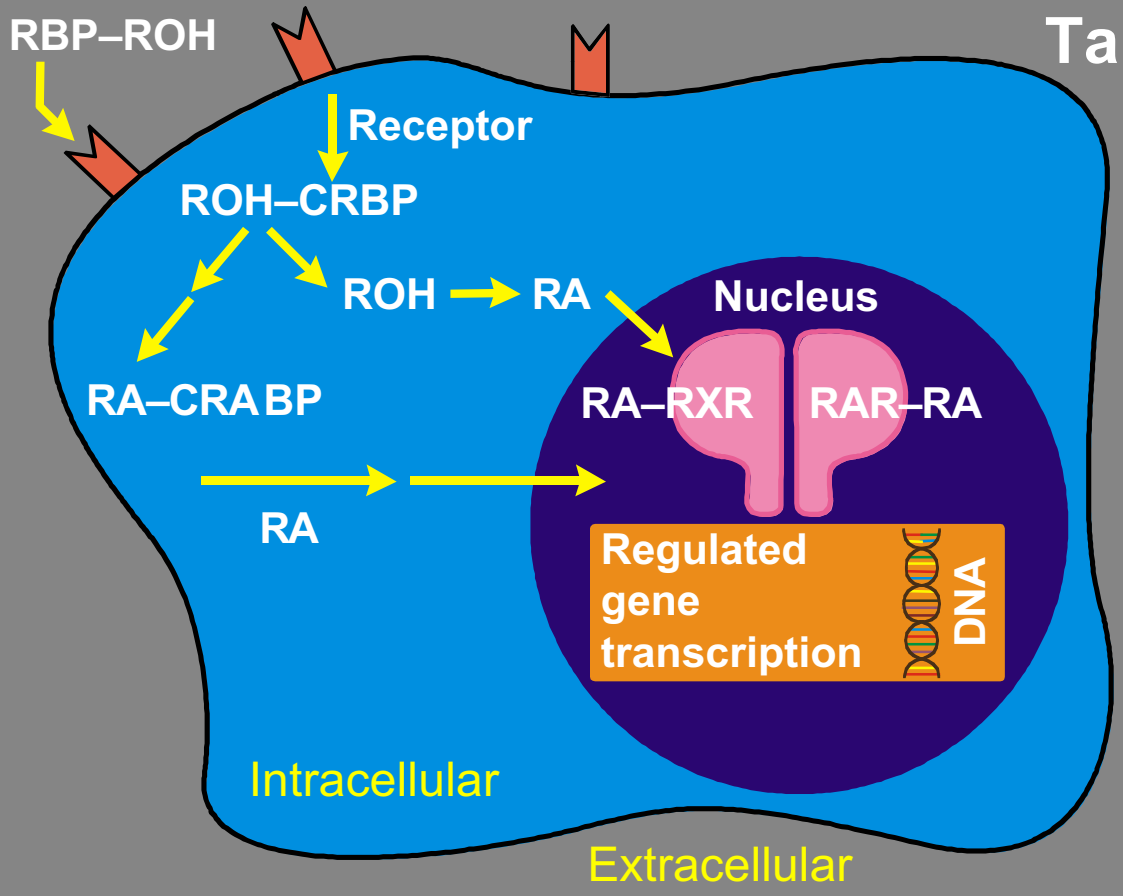
Carotenoid bioavailability factors

- Carotenoid species
- Concentration
- Food matrix
- Dietary fat etc.
- Parasites

Physiology


Liver
Parenchymal cells
Stellate cell (retinyl palmitate)
+ RBP
β-Carotene
Retinol
Small intestine
Chylomicrons
TTR
RBP
R
TTR
Eye (11-cis-retinal)
Other cells
Epithelia

Molecular biology



Target cell

ROH	=	Retinol
RA	=	Retinoic acid
RBP	=	Retinol binding protein
CRBP	=	Cellular retinol binding protein
CRABP	=	Cellular retinoic acid binding protein
RXR, RAR	=	Nuclear retinoic acid receptors

Functions

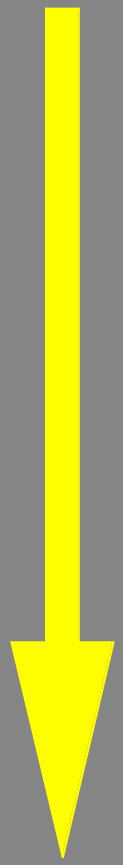
- Vision (night, day, colour)
- Epithelial cell integrity against infections
- Immune response
- Haemopoiesis
- Skeletal growth
- Fertility (male and female)
- Embryogenesis

Analytical methods

- Spectrophotometry (visual, UV)
- Spectrophotofluorometry
- High-performance liquid chromatography (HPLC)

Stages of deficiency

Increasing deficiency



Subclinical

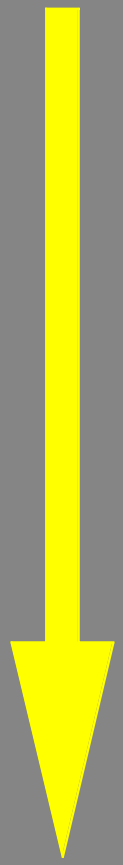
- **reducing stores**
- **lowering serum level**
- **metaplasia**

Clinical

- **xerophthalmia**
  - non-blinding
  - blinding

Tests of vitamin A status

Decreasing status



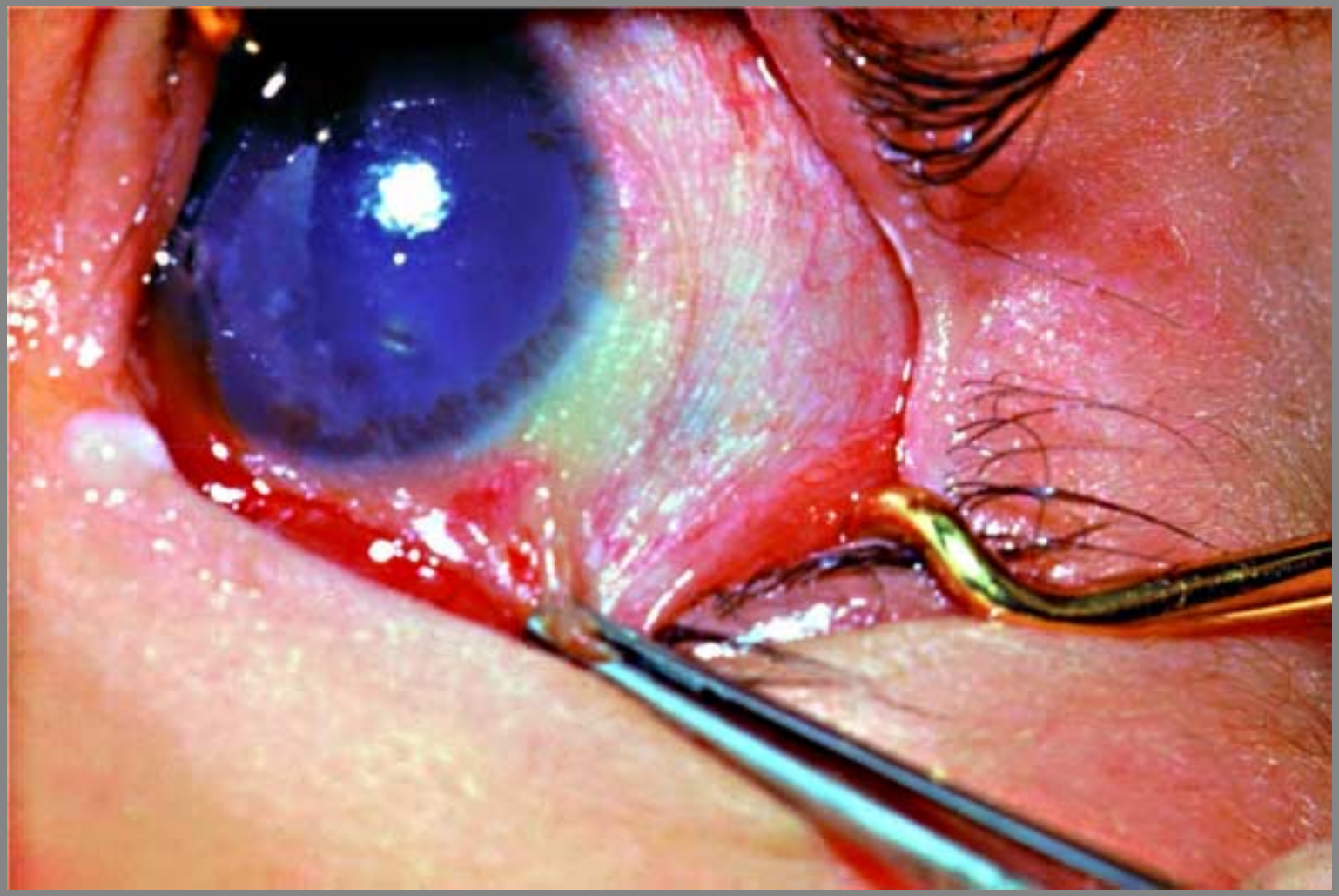
Subclinical

- relative dose-response test
- serum retinol
- retinal rod function
- conjunctival impression cytology (CIC)

Clinical

- night blindness
- conjunctival and corneal eye signs

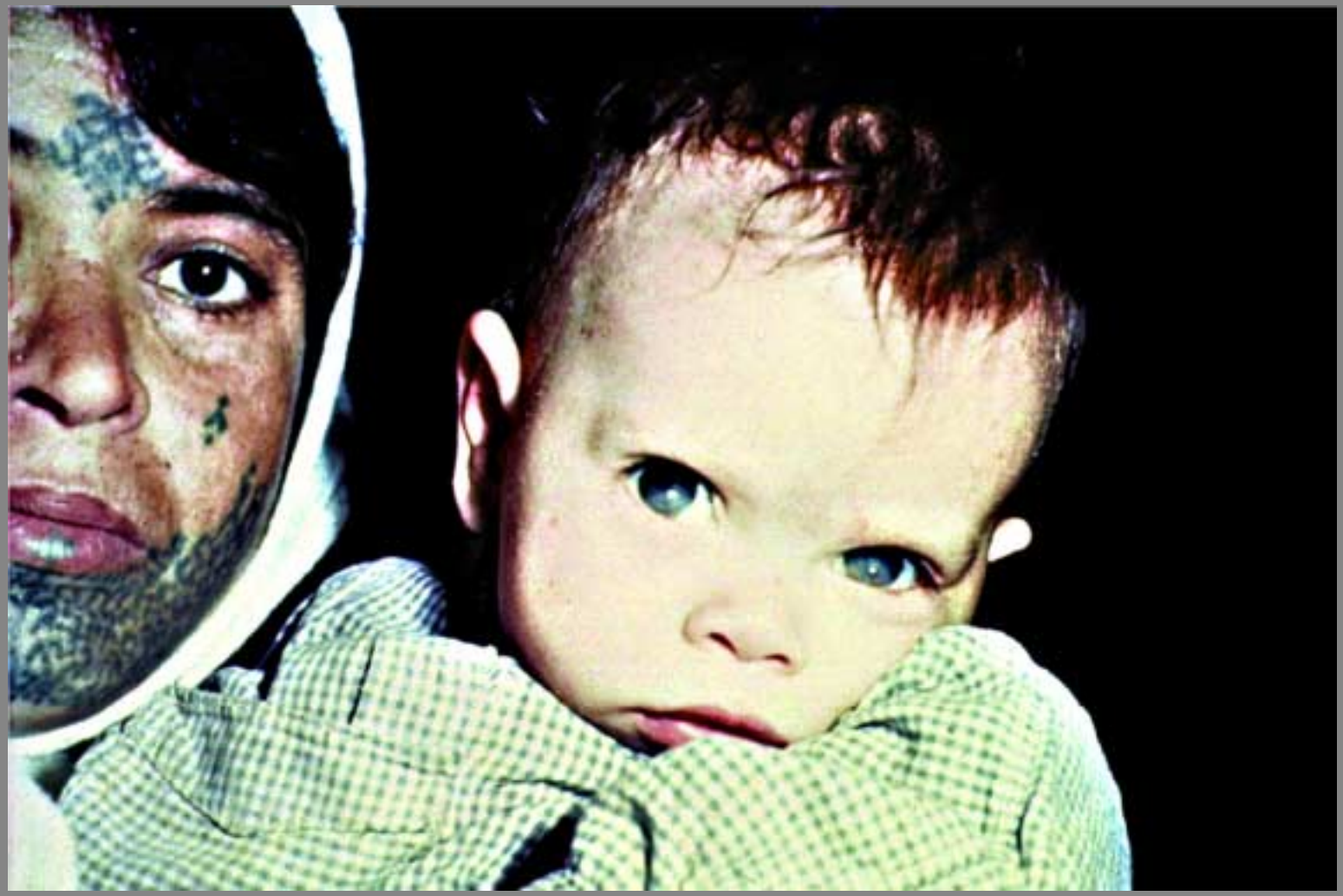
Conjunctival xerosis (X1A) and corneal xerosis (X2)



Bitot‘s spot (X1B)

Keratomalacia (X3A, X3B)

Corneal scarring (XS)



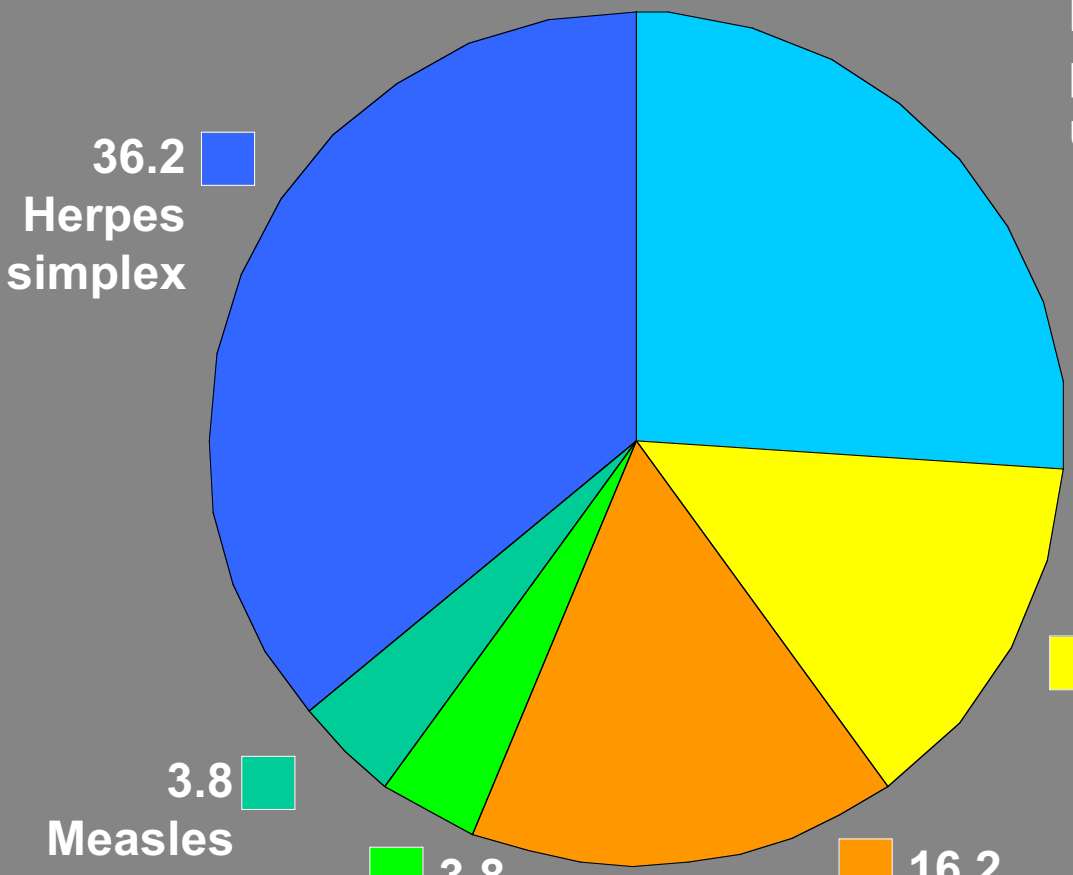
Xerophthalmia classification by ocular signs

- **Night blindness (XN)**
- **Conjunctival xerosis (X1A)**
- **Bitot‘s spot (X1B)**
- **Corneal xerosis (X2)**
- **Corneal ulceration/keratomalacia (X3A)**

  <1/3 of corneal surface
- **Corneal ulceration/keratomalacia (X3B)**

  ≥1/3 of corneal surface
- **Corneal scar (XS)**
- **Xerophthalmic fundus (XF)**

Corneal ulceration in children



Relative frequency of various primary causes of corneal ulceration in %

36.2 Herpes simplex

26.2 VAD

13.8 Traditional medicines

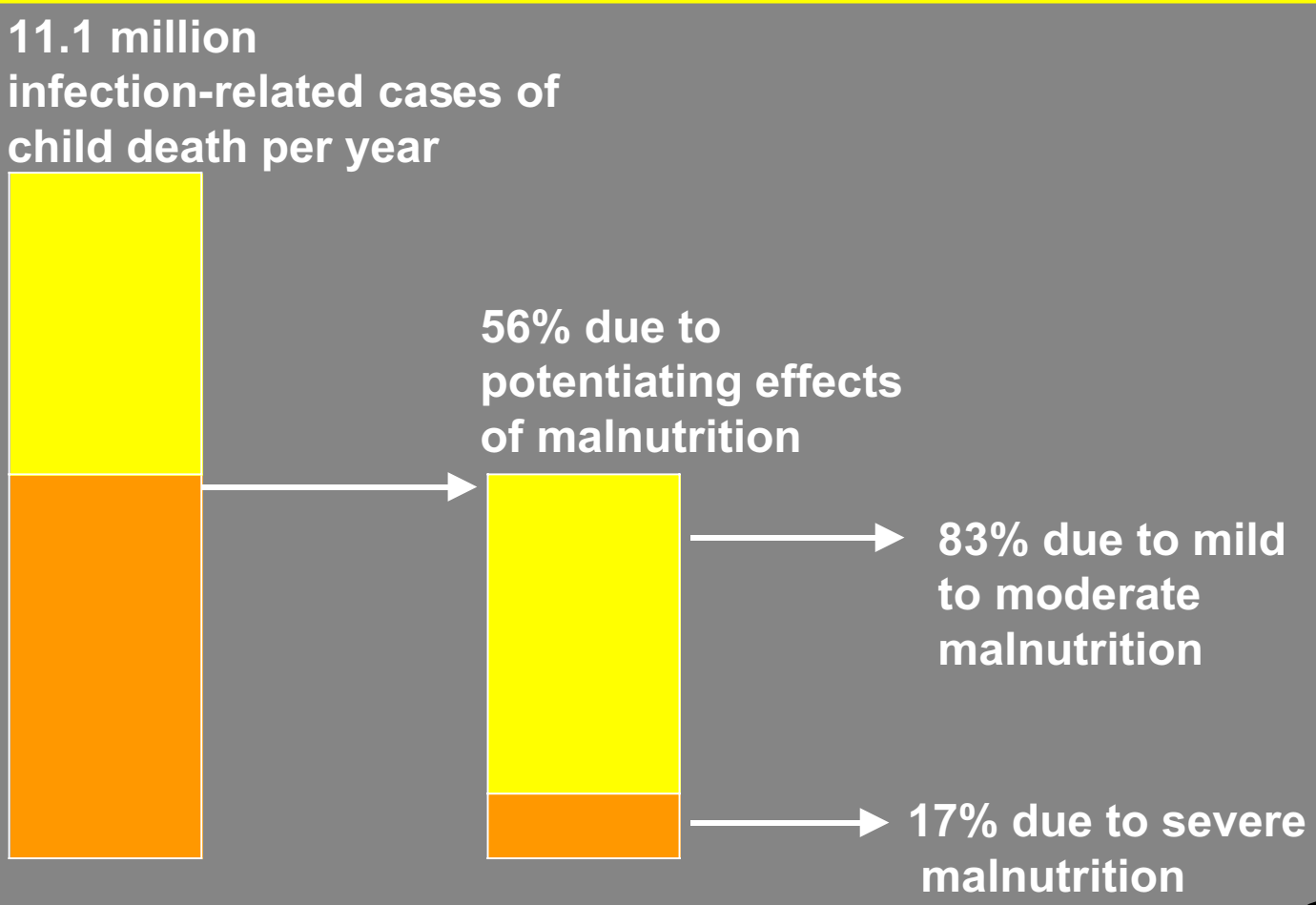
16.2 Other

3.8 Unknown

3.8 Measles

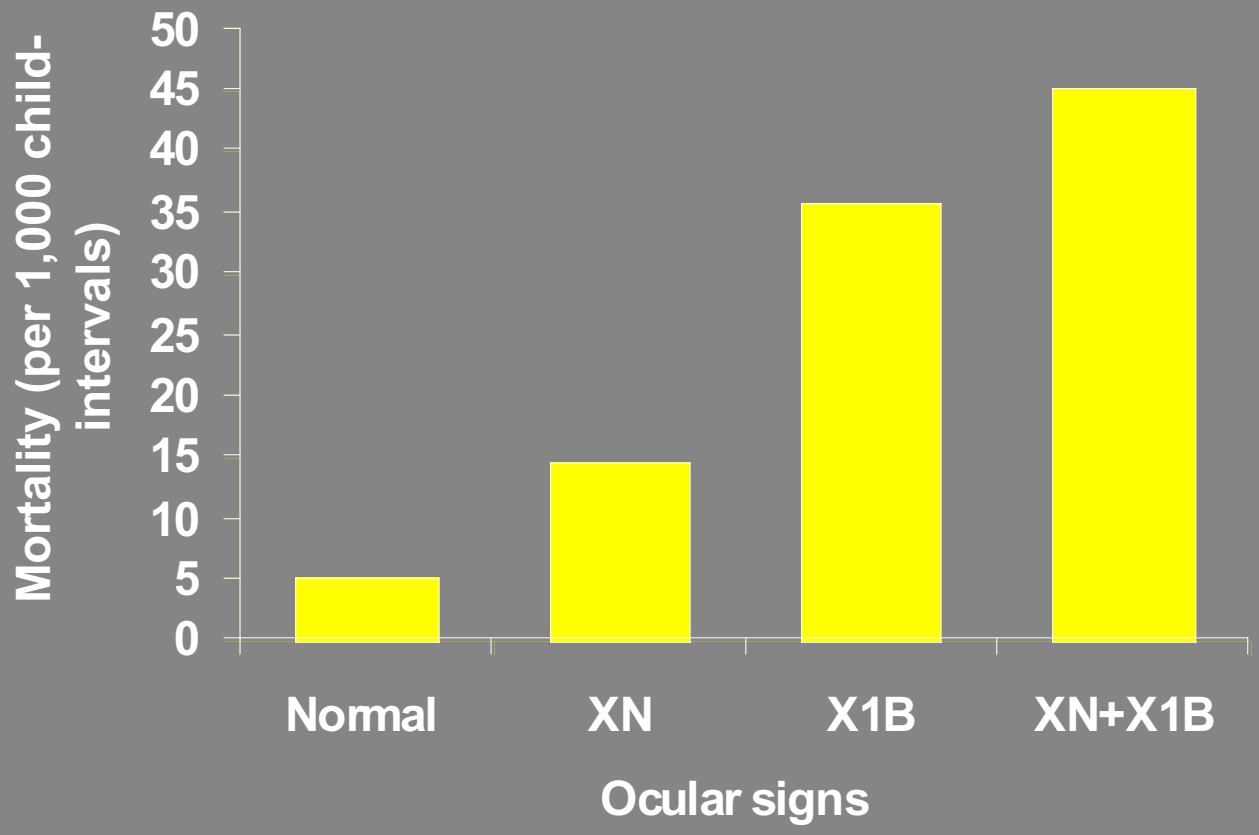
Foster and Sommer, 1987

Malnutrition and child death



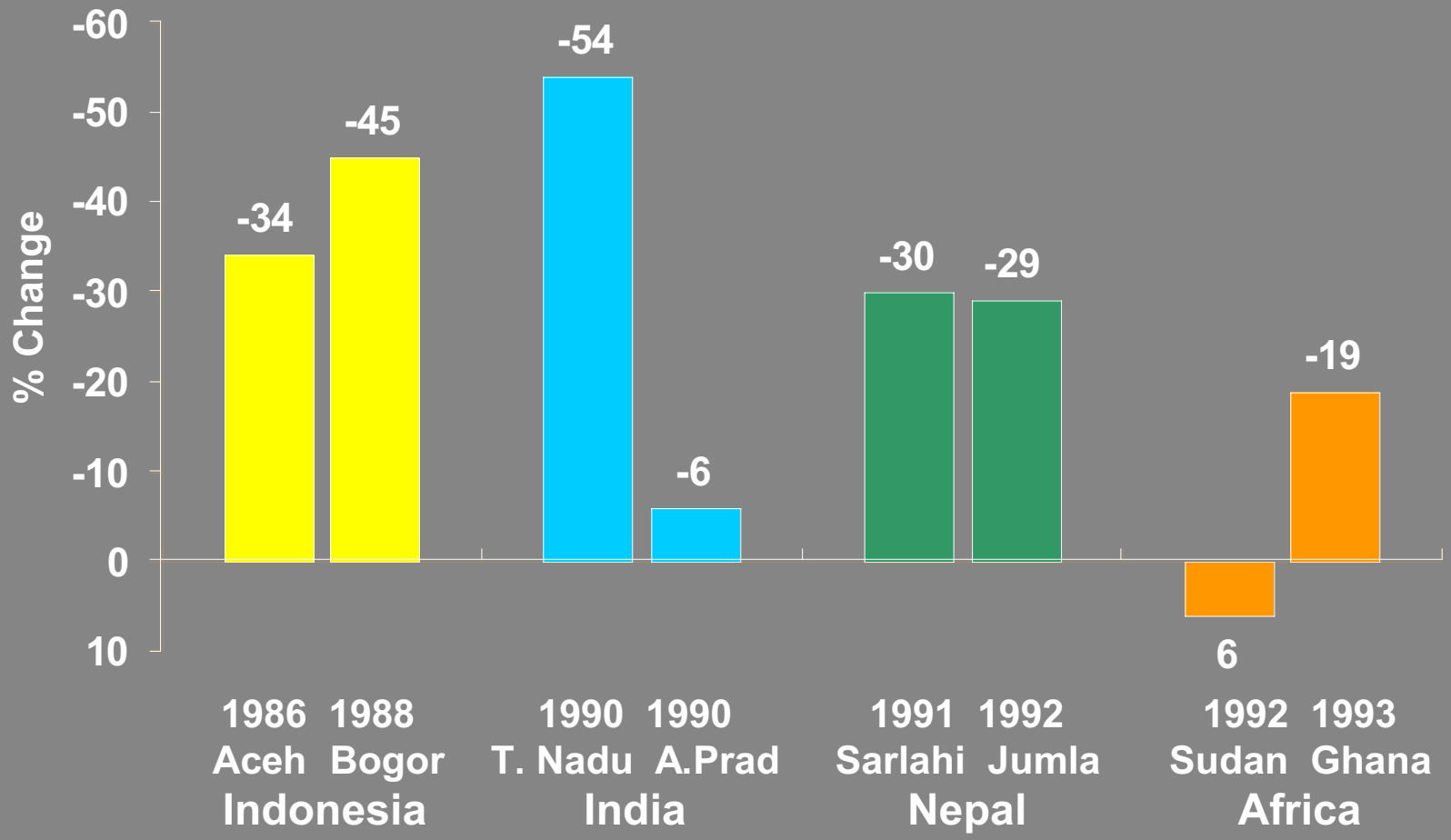
Pelletier et al, 1995

Association between VAD and mortality

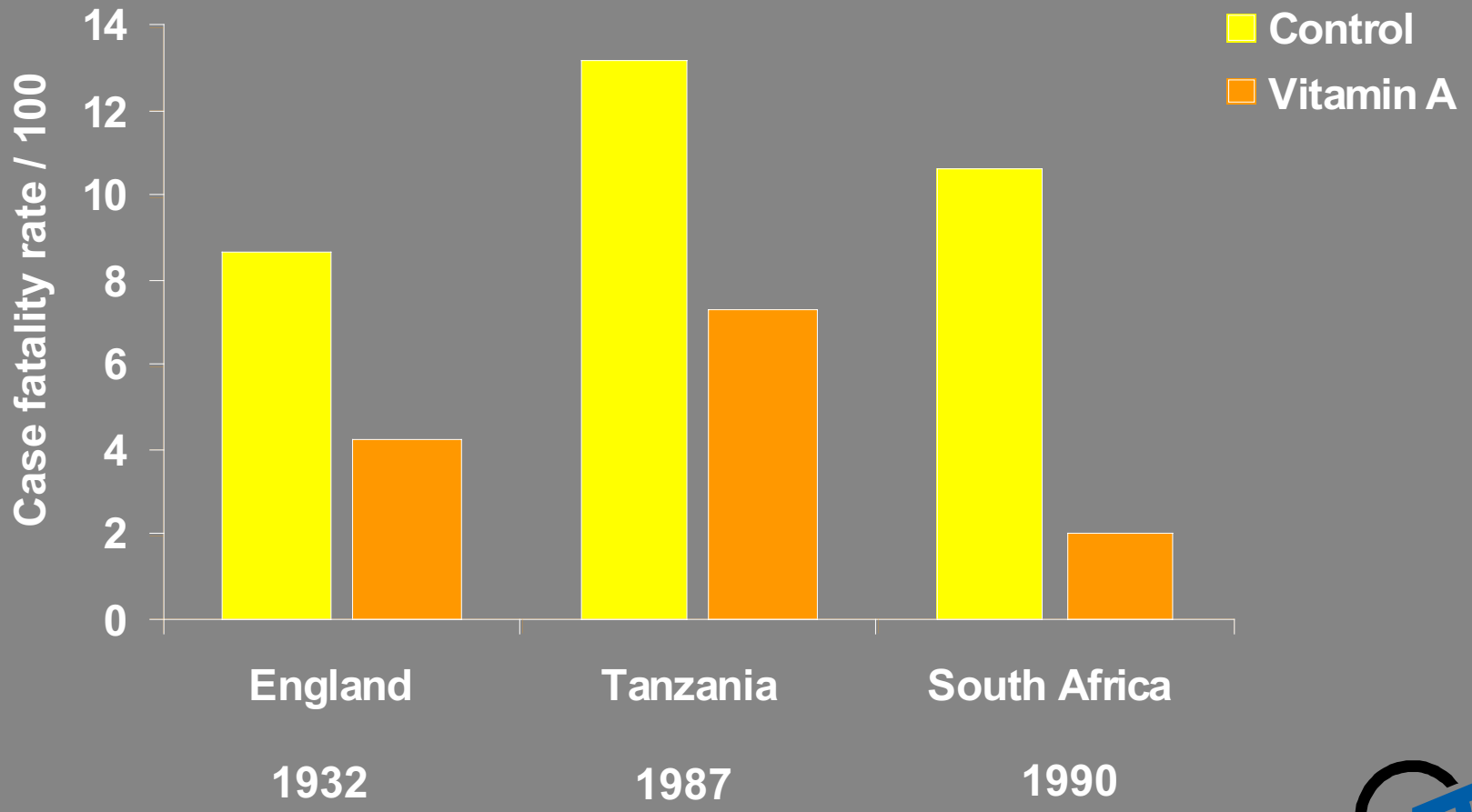


Sommer, Hussaini, Tarwotjo, 1983

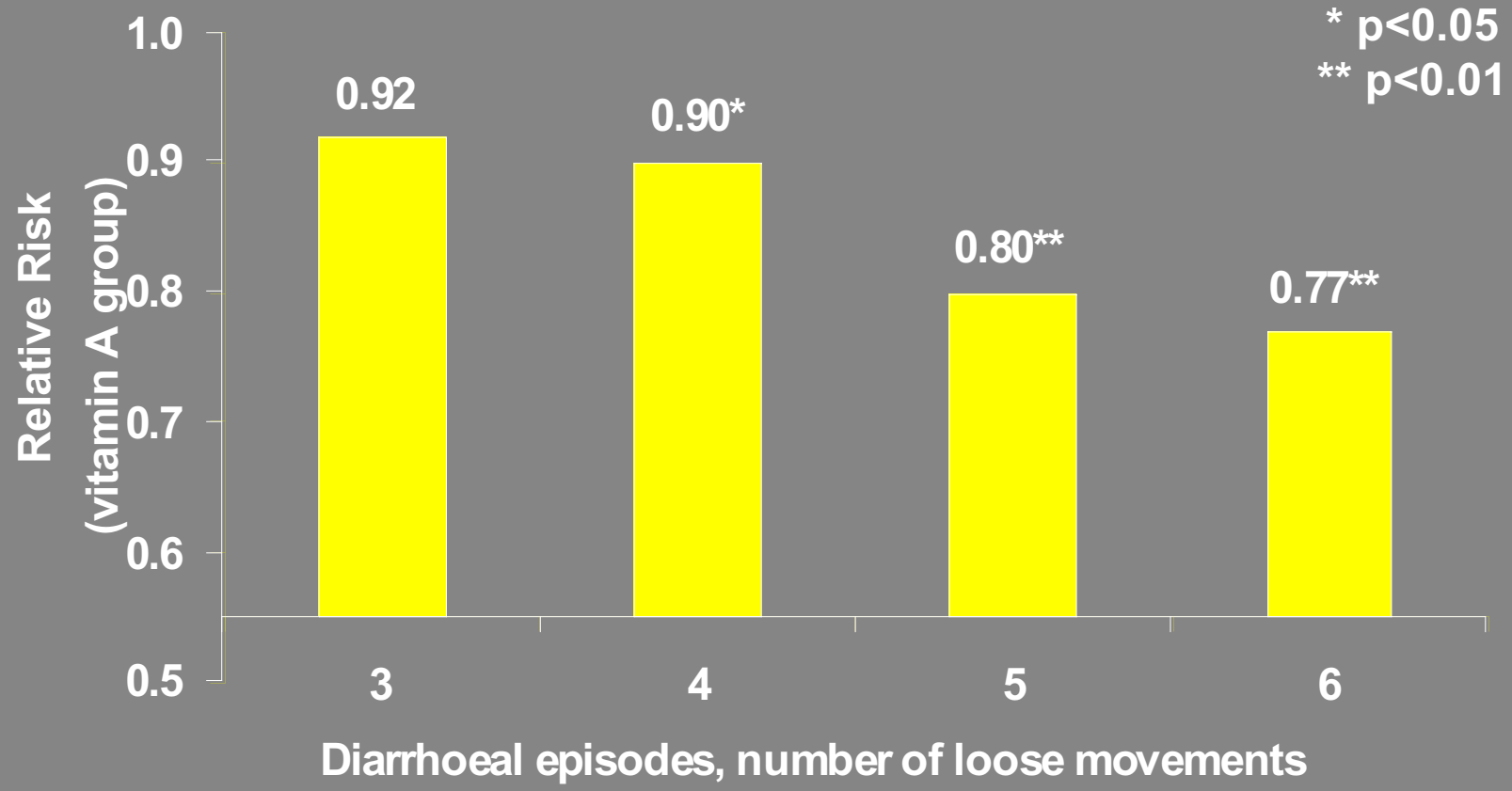
Impact of vitamin A on child mortality



Impact of vitamin A on measles mortality

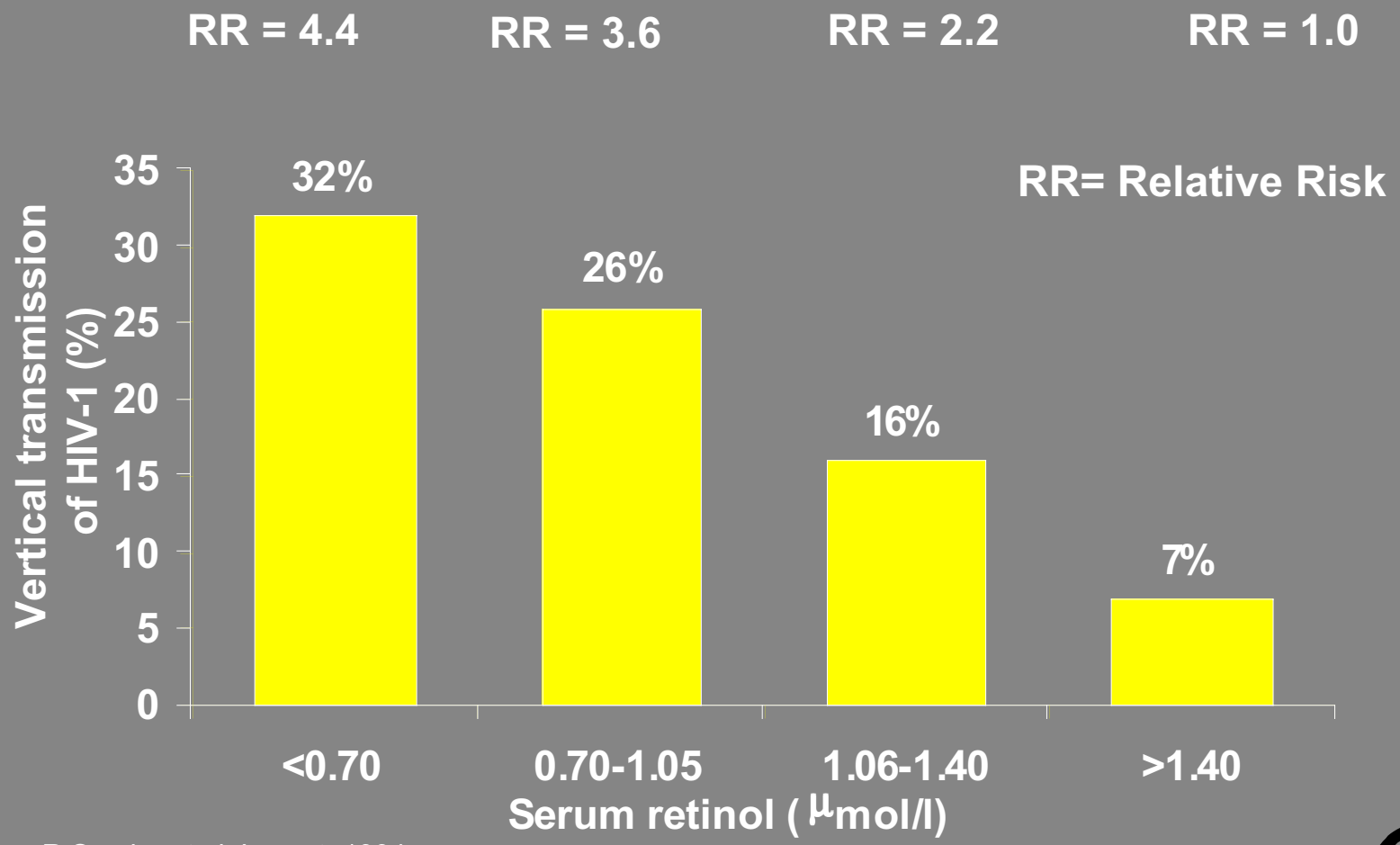


Impact of vitamin A on morbidity



Barrelo, Santos, Assis et al, 1994

Maternal HIV-1 infection and vitamin A status



Adapted from R.Semba et al, Lancet, 1994

Preliminary assessment of vitamin A status of a population

- Interviews by structured questionnaire
- Chart reviews
- Search for clinically active cases
- Search for old, healed disease
- Collect existing data on dietary intake and serum vitamin A levels

Sommer, 1995

WHO criteria of a public health problem of xerophthalmia

• Night blindness	(XN)	in >1%
• Bitot's spot	(X1B)	in >0.5%
• Corneal sclerosis/ ulceration/keratomalacia	(X2, X3A, X3B)	in >0.01%
• Corneal scar	(XS)	in >0.05%
• Plasma retinol of <0.35 µmol/l (10 µg/dl)		in >5%

WHO, 1992

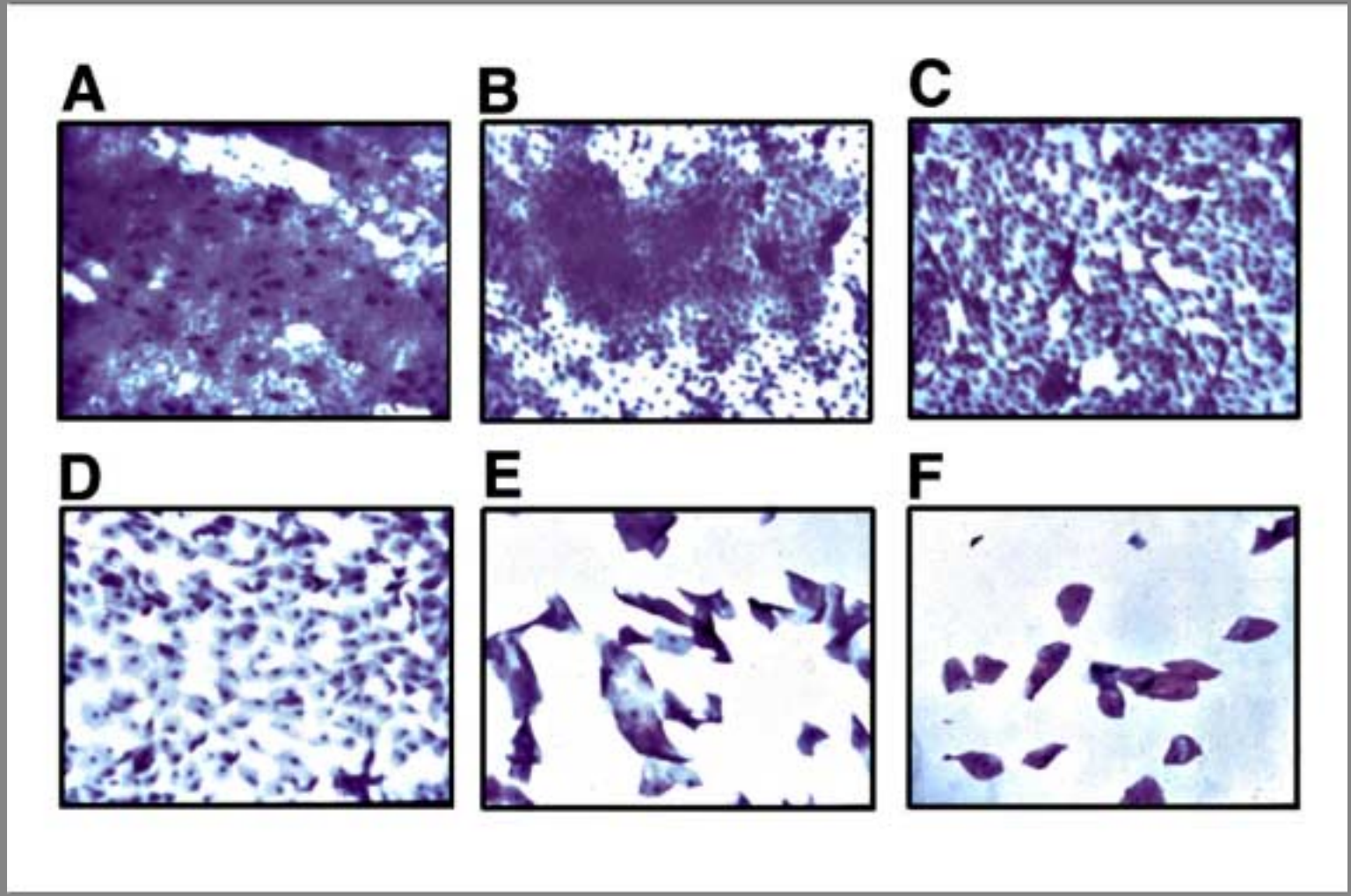
Biological indicators of subclinical vitamin A deficiency in children 6-71 months of age

Prevalence below cut-off to define a public health problem and its level of importance
*RDR = relative dose-response test

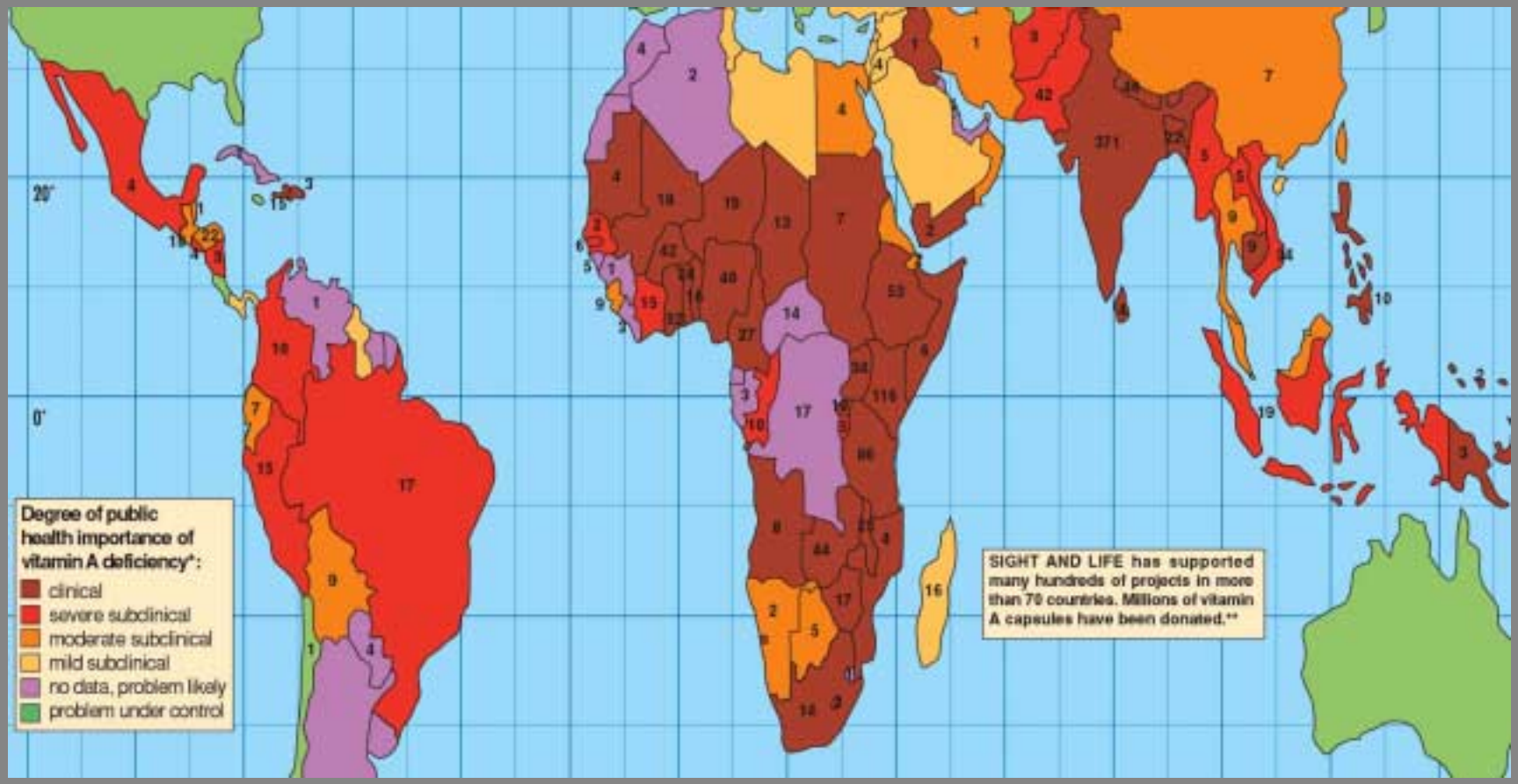
Indicator (cut-off)	Mild	Moderate	Severe
Functional			
Night blindness (present at 24 - 71 months)	>0 – <1%	≥1 – <5%	≥5%
Biochemical			
Serum retinol (≤0.7 µmol/l)	≥2 – <10%	≥10 – <20%	≥20%
Breast milk retinol (≤1.05 µmol/l)	≥2 – <10%	≥10 – <25%	≥25%
RDR (≥1.05 µmol/l)	≥5 – <20%	≥20 – <30%	≥30%

WHO, 1996 (modified)

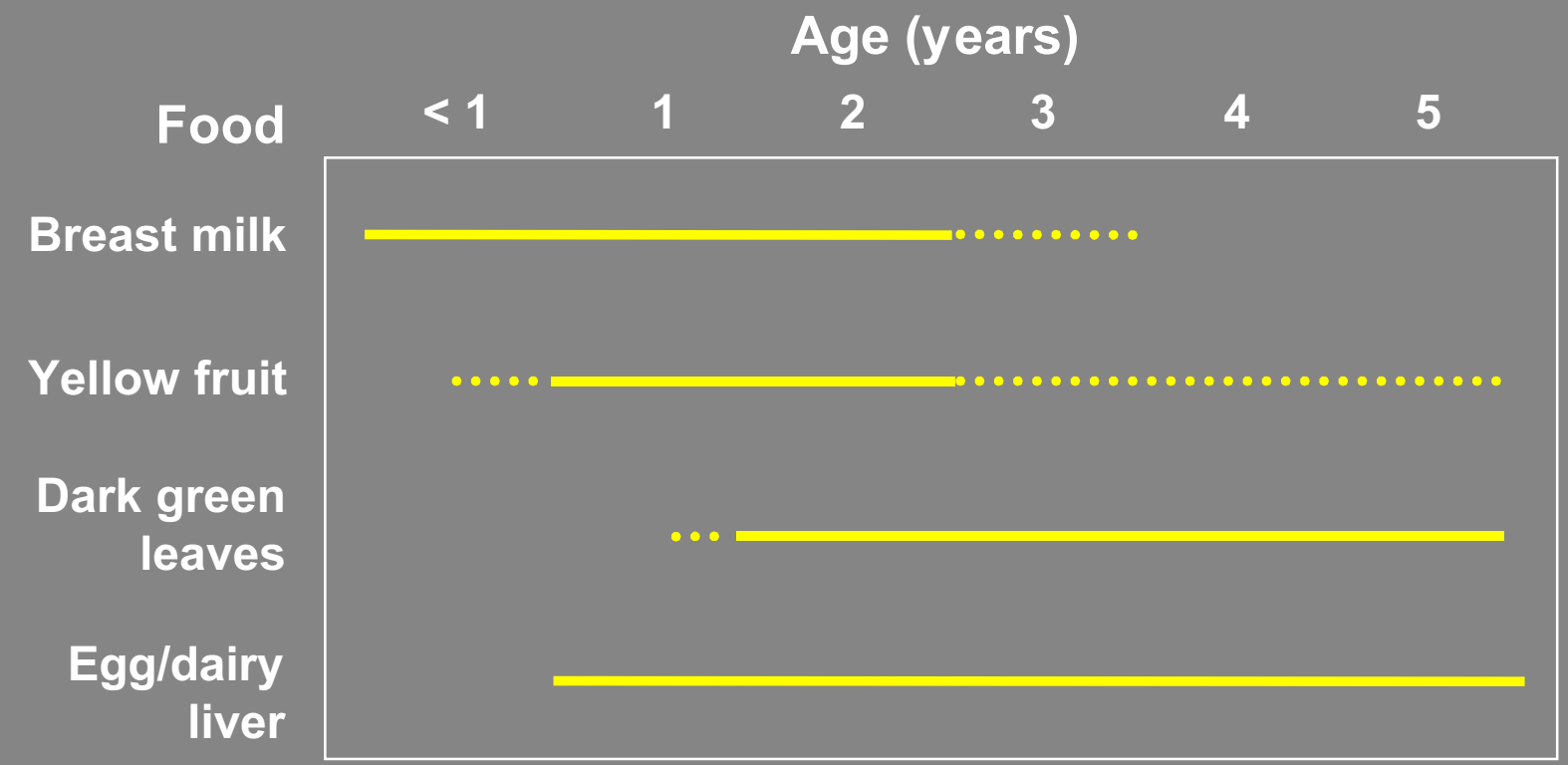
Histological indicator (CIC)



Global map of VADD

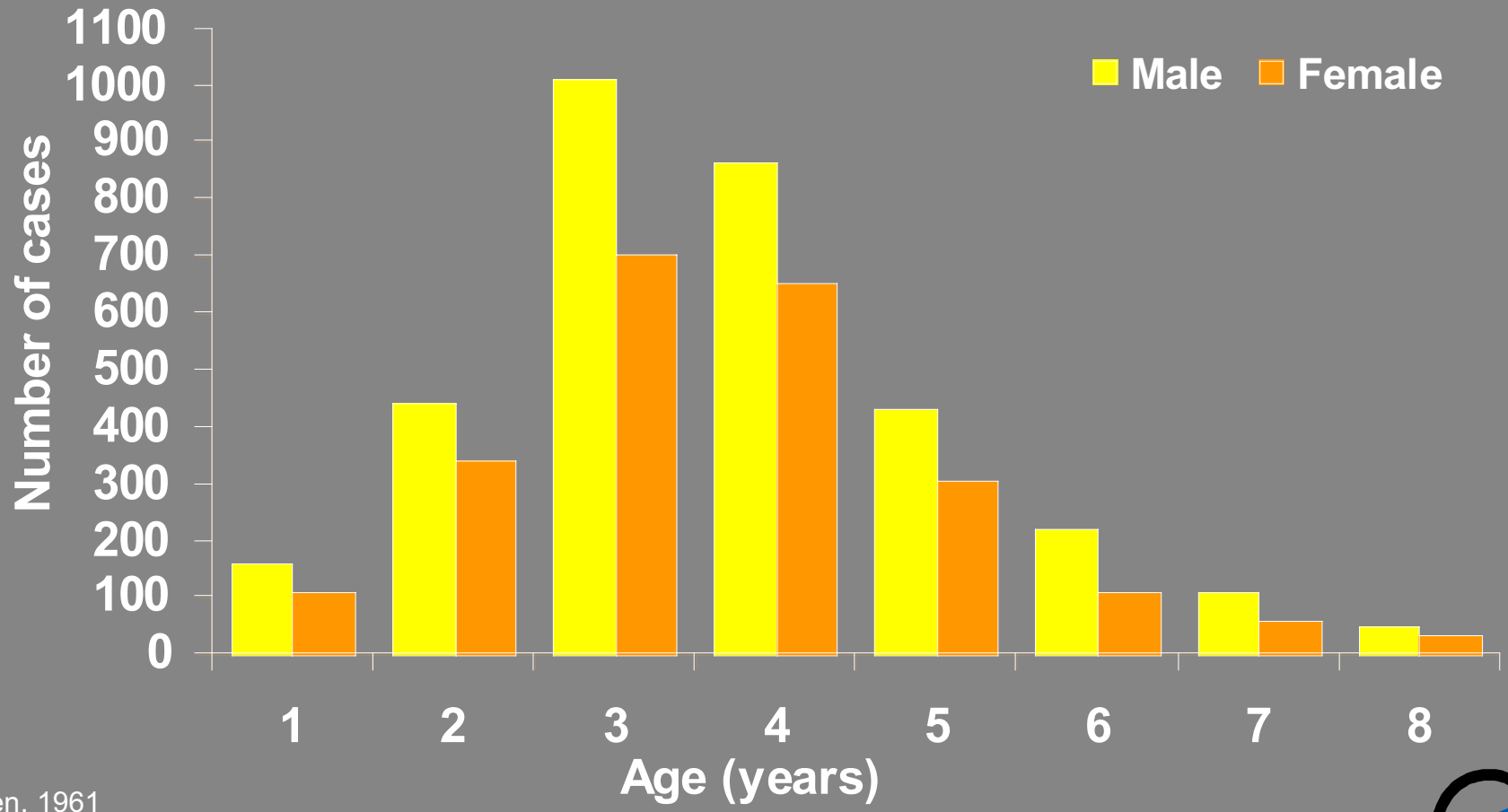


Protective effect of different food sources



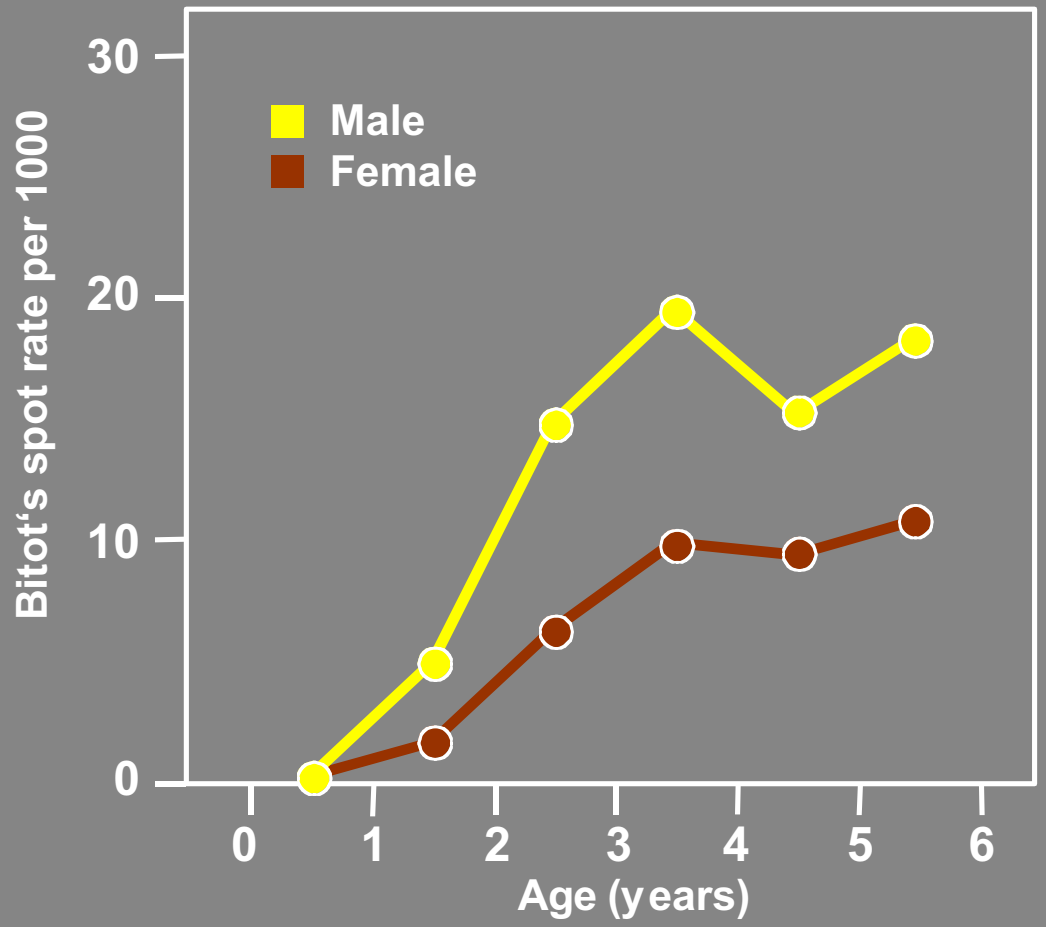
Sommer and West, 1996

VADD risk factors
1: Age



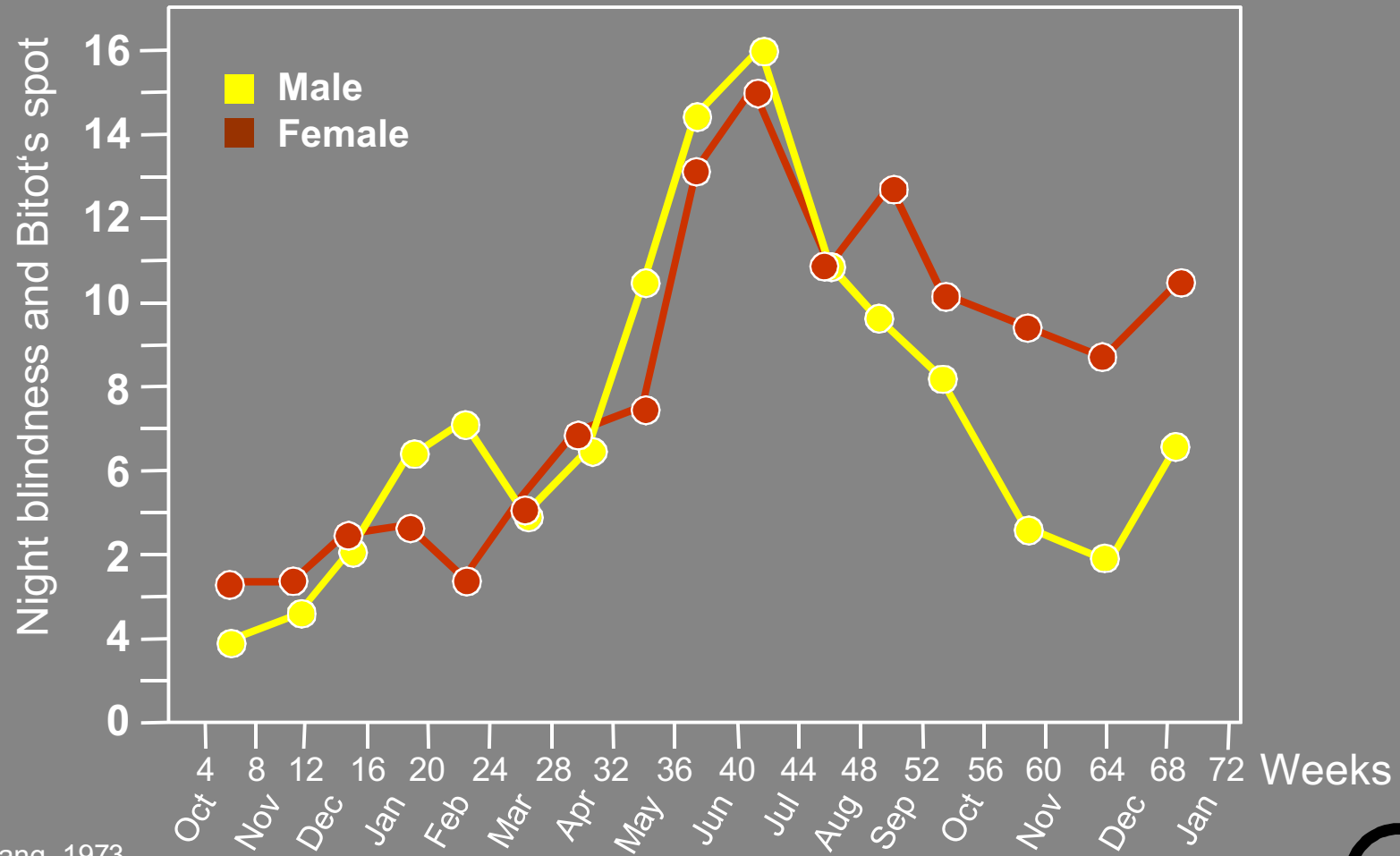
Oomen, 1961

VADD risk factors
2: Age and sex



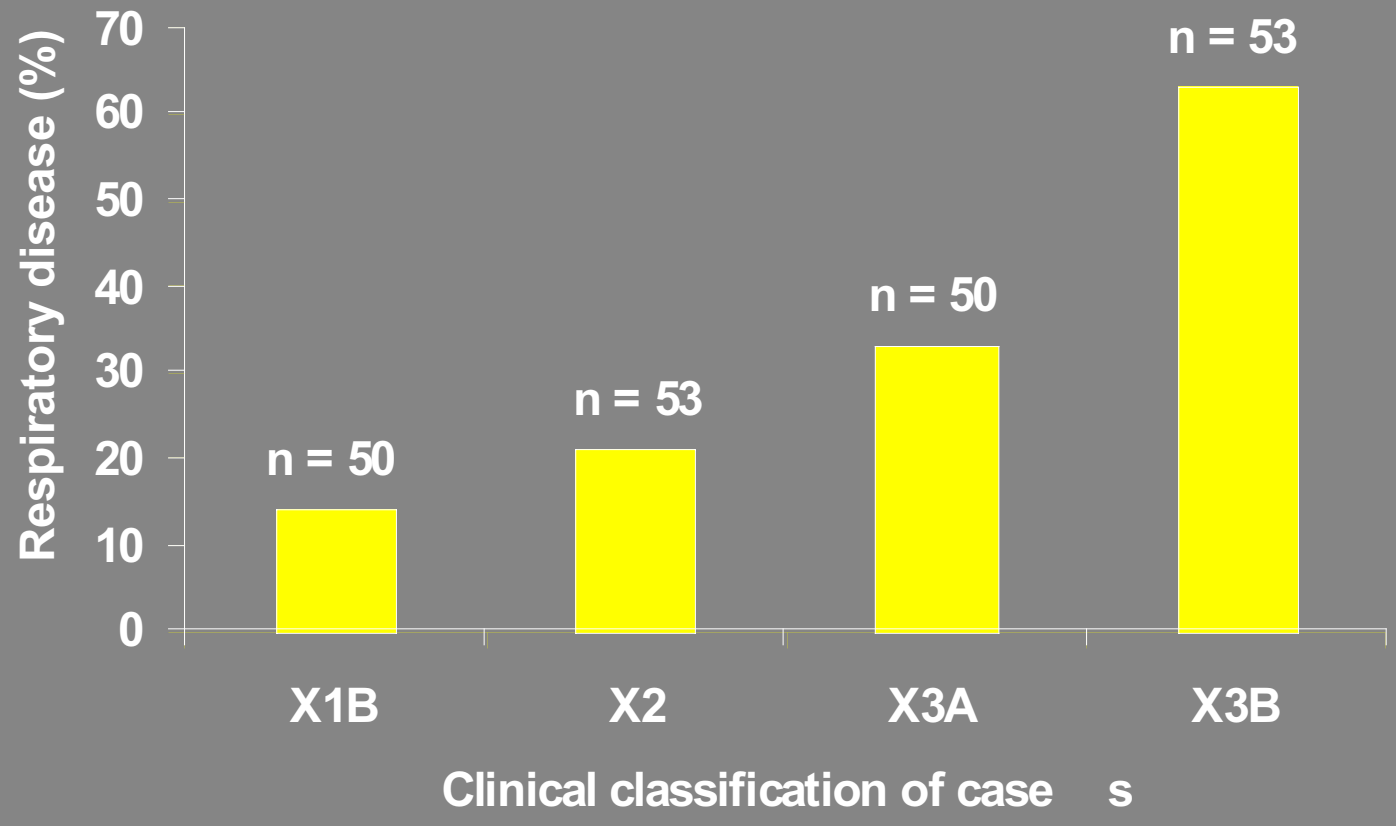
Sommer, 1982

VADD risk factors
3: Season



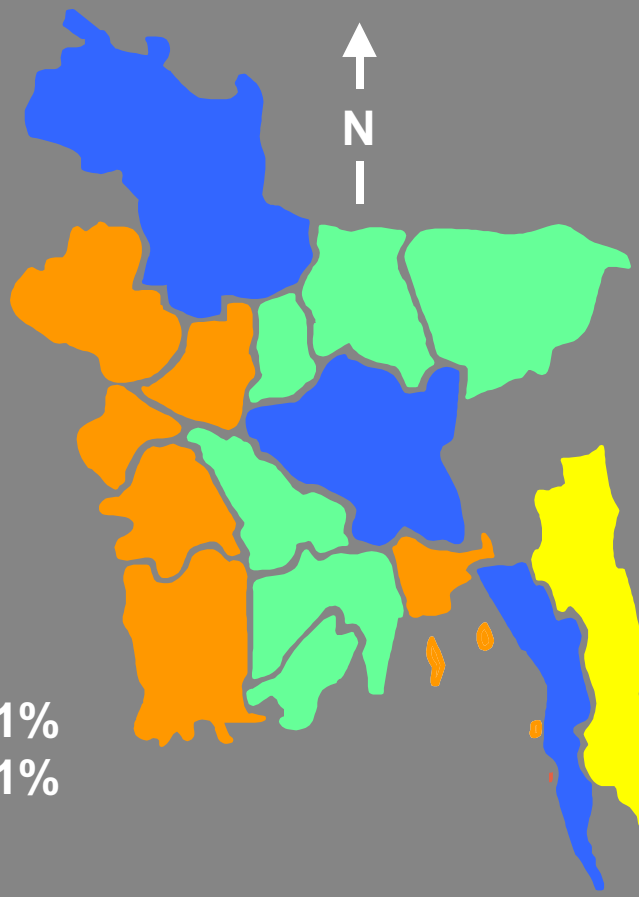
Sinha and Bang, 1973

VADD risk factors
4: Infectious diseases

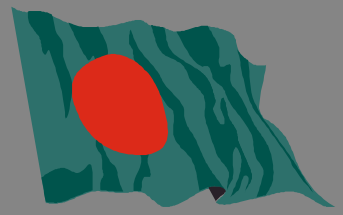


Sommer, 1982

VADD risk factors
5: Location



Bangladesh



X1B >1%
XN >3% and X1B <1%
XN <3% and X1B <1%
Not surveyed

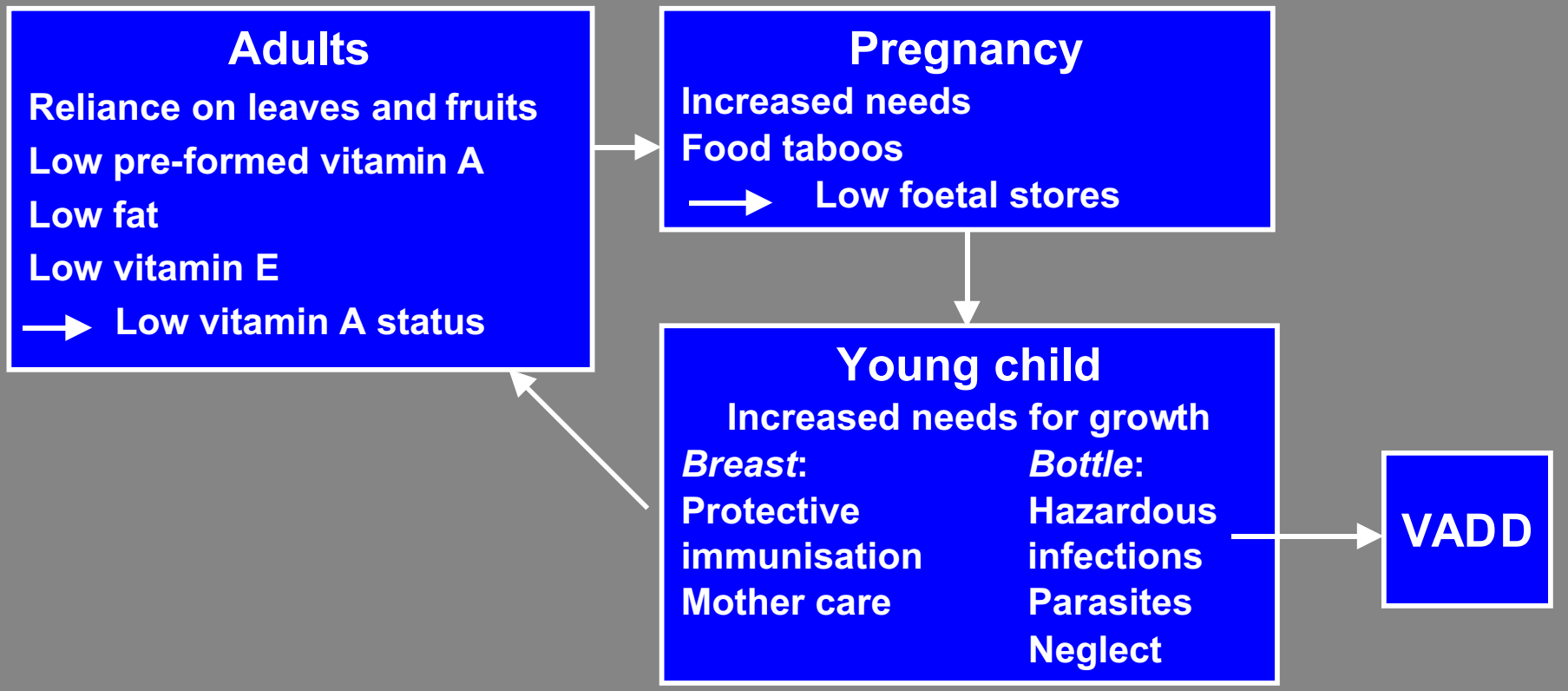
Cohen, Rahman, Mitra et al, 1987

VADD risk factors
6: Physiological status

Relative frequency of occurrence of eye signs

	XN	X1B	X2+3
Pre-school	+	+	++
School	++	++	+
Pregnancy	+++	+	
Lactation	+++	+	

The vitamin A deficiency disorders (VADD) cycle



Treatment schedule (orally)

Immediately on diagnosis:	
<6 months	**50,000 IU**
6-12 months	**100,000 IU**
>12 months	**200,000 IU**
Next day	**Same age-specific dose**
At least two weeks later	**Same age-specific dose**

WHO, 1997

Control of VADD

- Supplementation
- Fortification
- Diet diversification

- Infectious disease control
- Disaster relief
- Plant breeding

Prevention 1: Periodic oral supplementation

- **Infants <6 months** — **50,000 IU**
  Non-breast-fed infants, breast-fed infants whose mothers have not received supplemental vitamin A
- **Infants 6-12 months** — **100,000 IU**
  Every 4-6 months
- **Children >12 months** — **200,000 IU**
  Every 4-6 months
- **Mothers** — **200,000 IU**
  Within 8 weeks of delivery

WHO, 1997

A child receiving a vitamin A capsule

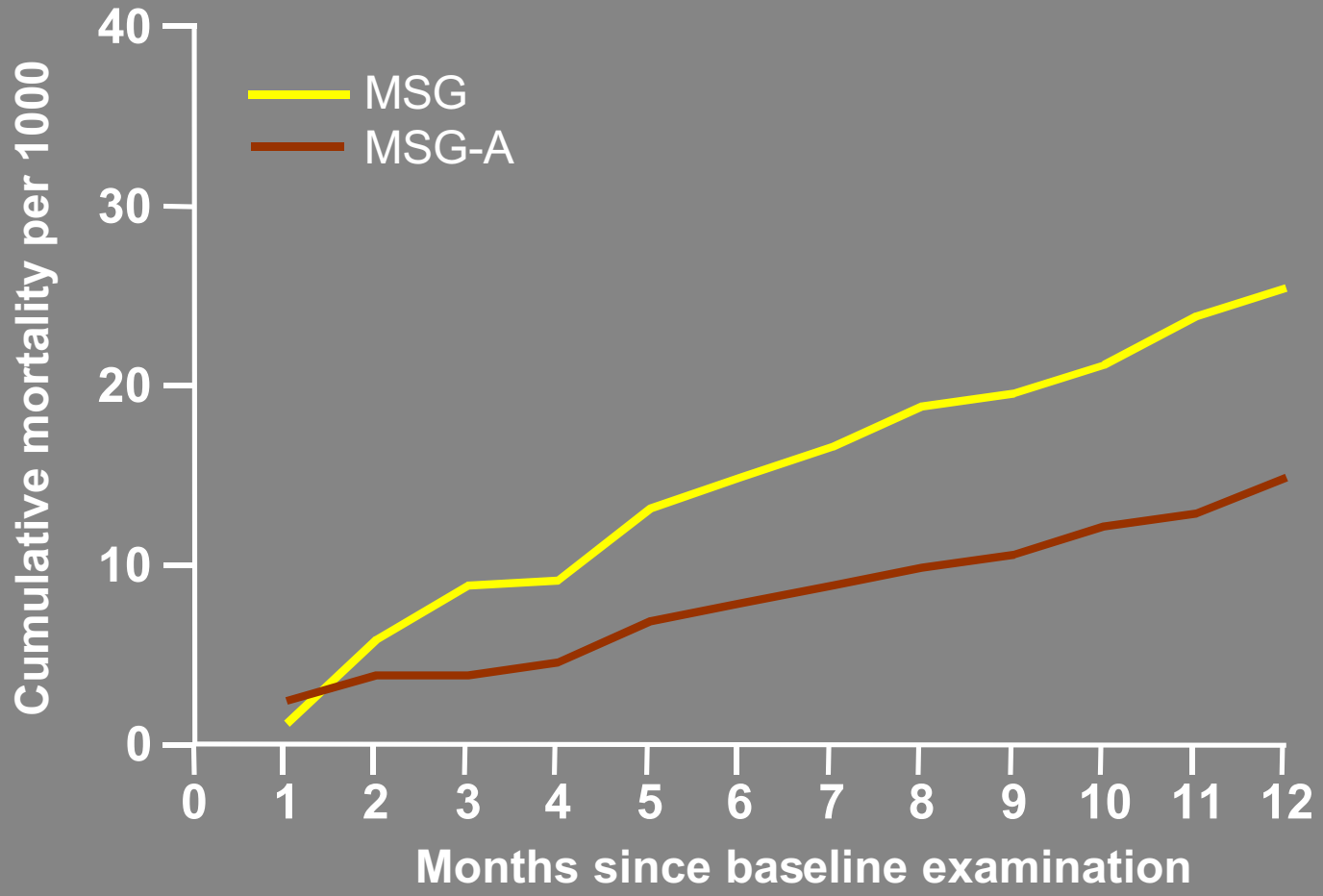
Prevention 2: Food fortification

Requirements

- Scientific rationale
- Industrial capacity
- Training
- Advocacy
- Legislative support
- Economic viability
- Community acceptance
- Sustainability
- Monitoring
- Quality control

Vitamin A-fortified sugar

MSG (monosodium glutamate) fortification trial Indonesia



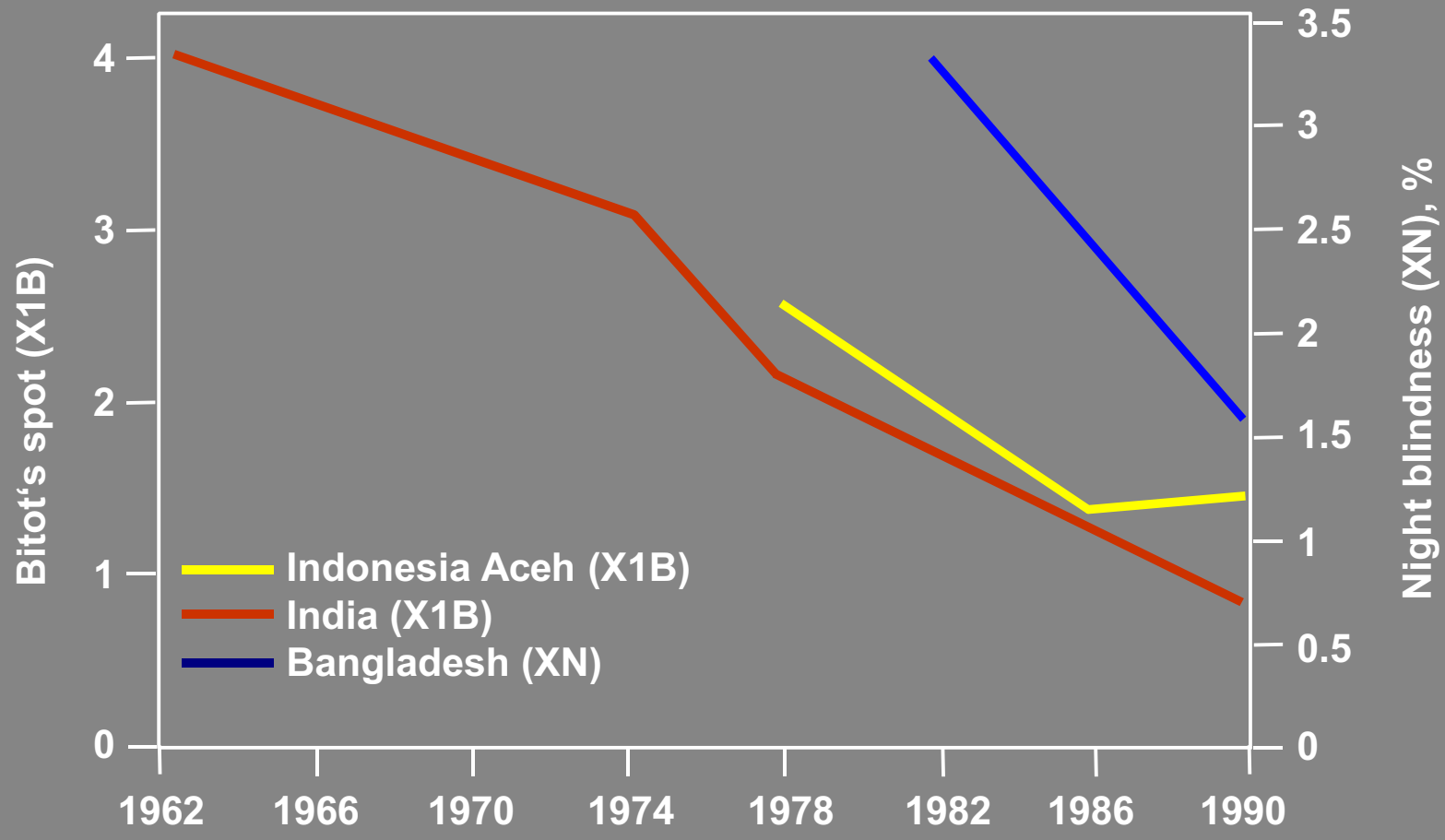
Sommer and West, 1996

Prevention 3: Dietary diversification

Advantages:	**Ultimate solution** **Community involvement** **Generating income** **Provides other nutrients**
Components:	**Production (home, school)** **Consumption** **(by vulnerable groups)**
Problems:	**Long-term cooperation** **Difficult in slums and desert areas**

Home gardening

Trends in xerophthalmia



Task Force SIGHT AND LIFE

PO Box 2116

4002 Basel, Switzerland

Tel.:	**+41 61 688 74 94**
Fax:	**+41 61 688 19 10**
E-mail:	**sight.life@roche.com**
homepage:	**www.sightandlife.org**