OVERVIEW - BIOLOGY OF TWINNING

1. Female estrus cycle, fertilization, early development of singleton births

2. Types of twins and the way they originate

3. Estimating heritability from twin studies
OVERVIEW - BIOLOGY OF TWINNING

1. Female estrus cycle, fertilization, early development of singleton births

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Fertilization and early development

Cleavage divisions: 2 cell stage (2 blastomeres)  
4 cell stage (4 blastomeres), etc
Fertilization and early development, cont’d

MORULA

BLASTOCYST
NORMAL SINGLETON DEVELOPMENT

- Inner cell mass (ICM)
- Chorion
- Amnion
- Embryonic disc (gives rise to single embryo)

Chorion
NORMAL FERTILIZATION AND DEVELOPMENT:

1. Usually only one egg is ovulated every month

2. Fertilization is by only one sperm

3. Baby has one amnion and one chorion
OVERVIEW - BIOLOGY OF TWINNING

1. Female estrus cycle, fertilization, early development of singleton births

2. Types of twins and the way they originate

3. Estimating heritability from twin studies
BIOLOGY OF TWINNING

1. Monozygotic, one egg, or identical twins
BIOLOGY OF TWINNING

1. Monozygotic, one egg, or identical twins

2. Dizygotic, two egg, or fraternal twins
### Table 8.3
Approximate twinning rates in different populations, ranked by DZ rate.

<table>
<thead>
<tr>
<th>Population</th>
<th>MZ</th>
<th>DZ</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AFRICAN</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nigerians</td>
<td>5</td>
<td>40</td>
</tr>
<tr>
<td>South African</td>
<td>5</td>
<td>22</td>
</tr>
<tr>
<td>blacks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>U.S. blacks</td>
<td>4</td>
<td>12</td>
</tr>
<tr>
<td><strong>CAUCASIAN</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Italians</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>Swedes</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>U.S. whites</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td><strong>ASIANS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Koreans</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Chinese</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Japanese</td>
<td>5</td>
<td>3</td>
</tr>
</tbody>
</table>

\(^a\) Data are average values primarily from tables in Bulmer (1970).

MZ constant among populations

DZ varies with population,
Suggesting that the tendency for DZ twinning has a genetic basis
BIOLOGY OF TWILLNING: how twins originate

1. Monozygotic, one egg, or identical twins

2. Dizygotic, two egg, or fraternal twins
KINDS OF MONOZYGOTIC TWINS

1. Zygote divides into two separate cells (embryos) at first cleavage division
Monozygotic (one egg) twins
Monzygotic (one egg) twins

ZYGOTE

first division
Monzygotic (one egg) twins

zygote → first division → separation
Monzygotic (one egg) twins

ZYGOTE

first division

separation

Embryo

Embryo
Armadillo

Indentical Quadruplets
KINDS OF MONOZYGOTIC TWINS

1. Zygote divides into two separate cells (embryos) at first cleavage division

2. Two inner cell masses develop and each gives rise to a separate embryo
MONOZYGOTIC (one egg) TWINS

2 inner cell masses, 2 embryonic discs

1 inner cell mass, 2 embryonic discs

Fig. 53. Two types of monozygotic twinnning in man: (a) by formation of two inner cell masses; (b) by formation of two embryos on a single germ disc. From G. W. Corner, Bull. Johns Hopkins Hosp., 35 (1923) 389.
KINDS OF MONOZYGOTIC TWINS

1. Zygote divides into two separate cells (embryos) at first cleavage division

2. Two inner cell masses develop and each gives rise to a separate embryo

3. A single inner cell mass forms but later divides, giving rise to two embryos
MONOZYGOTIC (one egg) TWINS

2 inner cell masses, 2 embryonic discs

1 inner cell mass 2 embryonic discs

Fig. 5.3. Two types of monzygotic twinning in man: (a) by formation of two inner cell masses; (b) by formation of two embryos on a single germ disc. From G. W. Corner, Bull. Johns Hopkins Hosp., 35 (1923) 389.
KINDS OF MONOZYGOTIC TWINS

1. Zygote divides into two separate cells (embryos) at first cleavage division

2. Two inner cell masses develop and each gives rise to a separate embryo

3. A single inner cell mass forms but later divides, giving rise to two embryos

4. A single inner cell mass forms, divides incompletely, and Siamese twins are formed
MONOZYGOTIC (one egg) TWINS

2 inner cell masses, 2 embryonic discs
1 inner cell mass, 2 embryonic discs

Siamese twins: separation of the two embryonic discs is incomplete and the twins are joined at some place.
NORMAL FERTILIZATION AND DEVELOPMENT:
1. Usually only one egg is ovulated every month
2. Fertilization is by only one sperm
3. Baby has one amnion and one chorion

DIZYGOTIC TWINS
1. More than one egg is ovulated and fertilized
   (more in the case of triplets, etc, fertility drugs)
2. May be same or opposite sex, because different sperm
   fertilize different eggs
3. Two chorions, two amnions
4. Incidence may be increased by genetic predisposition,
   maternal age, or fertility drugs
Issues in estimating heritability from for human traits: from twin studies

1. Are twins representative of the general population?

2. Twins treated differently by family, teachers, depending upon zygosity (MZ or DZ)?

3. Measures made at same age for both members of a twin pair

4. DZ twins same sex or opposite sex?
<table>
<thead>
<tr>
<th>Weeks of gestation</th>
<th>Twins</th>
<th>Singletons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 28 weeks</td>
<td>4.0</td>
<td>0.5</td>
</tr>
<tr>
<td>28-31 weeks</td>
<td>5.2</td>
<td>0.8</td>
</tr>
<tr>
<td>32-35 weeks</td>
<td>10.8</td>
<td>1.9</td>
</tr>
<tr>
<td>36 weeks</td>
<td>12.7</td>
<td>8.4</td>
</tr>
<tr>
<td>37-39 weeks</td>
<td>14.9</td>
<td>8.8</td>
</tr>
<tr>
<td>40 weeks</td>
<td>51.4</td>
<td>76.4</td>
</tr>
<tr>
<td>41 weeks and over</td>
<td>1.1</td>
<td>3.2</td>
</tr>
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</table>
Genetics and Mental Health

Schizophrenia

Affective disorder
DSM IV Diagnostic Criteria for Schizophrenia

A. Characteristic psychotic symptoms of types (1), (2), or (3)
   1. Two of the following:
      a. Delusions
      b. Hallucinations
      c. Loosening of associations or incoherence
      d. Catatonic behavior
      e. Flat or grossly blunted affect
   2. Bizarre delusions (thought broadcasting, controlled by a dead person)
   3. Prominent hallucinations: a voice keeping up a running commentary on the persons behavior or thoughts, or two or more voices conversing

B. Functioning at work, social/family settings impaired; decline in self care

C. Other disorders ruled out

D. Symptoms present for at least six months
Diagnostic criteria for Schizophrenia
Before and after “active” episodes, may be observed:

1. Marked social isolation or withdrawal

2. Impaired function as wage-earner, home-maker, student

3. Peculiar behavior: collecting garbage, food hoarding, talking to self publicly

4. Impaired personal hygiene and grooming

5. Odd or magical beliefs, clairvoyance, telepathy

6. Unusual perceptual experiences: sensing presence of a force or person not actually present

7. Marked lack of initiative, energy, or interests
Subtypes of schizophrenia

1. **Catatonic type**: rigid, lack of movement, strange posturing

2. **Disorganized type**: incoherence, inappropriate affect

3. **Paranoid type**: preoccupation with systematized delusions, frequent auditory hallucinations

4. **Undifferentiated type**: combination of all above symptoms
Epidemiology of schizophrenia

1. Incidence is 1% general population

2. Sex ratio equal, but males have an earlier age at onset (19 versus 22)

3. Familial
Incidence of schizophrenia is higher in people who are related to a schizophrenic.

- Unrelated person (0%): 1%
- Spouse (0%): 2%
- Nephew or niece (25%): 3%
- Sibling (50%): 10%
- Offspring of one patient (50%): 13%
- Fraternal twin (50%): 14%
- Offspring of two patients:
  - 46%
- Identical twin (100%): 46%

Percentage risk of developing schizophrenia
Schizophrenia as a quasicontinuous trait: the more genetic factors present, the greater the genetic liability

1. Earlier age of onset is associated with poor prognosis (as predicted if the genetic liability were greater)

2. Parents with more severe schizophrenia have a higher risk of having affected children (as predicted if the genetic liability were greater)
Affective Disorders (Mood Disorders)

1. Depression

2. Bipolar Disorder (Manic – Depression)

3. Unipolar disorder (Depression)
Epidemiology of Affective Disorder

1. About 1-5% of general population
2. Slightly more females than males
3. Familial component
DSM IV: Bipolar Disorder

1. At least one manic episode
2. Usually followed by depressive episode
3. May cycle between manic and depressive episodes
DSM IV  Diagnostic Criteria for Manic Episode

A. Period of abnormally elevated, expansive or irritable mood
B. During period of mood disturbance, at least 3 of the following
   1. Inflated self esteem or grandiosity
   2. Decreased need for sleep (3 hrs may suffice)
   3. Highly talkative
   4. Thoughts are racing
   5. Distractible
   6. Increased goal directed activity or psychomotor agitation
   7. Buying sprees, sexual promiscuity, foolish investments
C. Mood disturbance impairs work or social relationships
D. Not schizophrenia or other psychosis
E. Not induced by substance
DSM IV Diagnostic Criteria for Depression

A. At least 5 of the following for at least 2 weeks
   1. Depressed mood most of the day nearly every day
   2. Diminished interest in daily activities
   3. Significant weight loss or gain (appetite change)
   4. Insomnia or hypersomnia every day
   5. Psychomotor agitation or retardation every day
   6. Fatigue or energy loss every day
   7. Inability to think or concentrate, indecisiveness
   8. Recurrent thoughts of death
   9. Feelings of worthlessness

B. Not caused by an organic factor (drug or injury)
C. Not in response to death of a loved one (bereavement)
D. No evidence of hallucinations, delusions (schizophrenia)
Mode of inheritance affective disorder:

1. One or more genes of major effect: affected person has higher probability of producing an affected child than seen in schizophrenia. From 25% to 50%, depending on the study.

2. May show reduced penetrance (not every individual with the gene or genes exhibits the condition.)
Drug therapy for depression

**Tricyclics:** Elavil, Anafranil, Norpramin, Sinequan
Tofranil, Pamelor, Vivactil, Surmontil

**Heterocyclics:** Asendin, Wellbutrin, Ludlomil, Desyrel

**Selective serotonin re-uptake inhibitors (SSRIs):** Prozac, Paxil, Luvox, Celexa, Zoloft, Lexapro

**Other compounds:** Remeron, Serzone, Effexor

**Monoamine oxidase inhibitors (MOIs):** Nardil, Parnate
Implications of drug therapy effectiveness for understanding the genetic basis of psychiatric conditions

1. The two major psychoses respond to entirely different classes of therapeutic drugs

   Different sets of genes underlie vulnerability to each condition

2. Among patients with the same diagnosis, there are differences in the responsiveness to different drugs.

   A given condition, such as schizophrenia, exhibits genetic heterogeneity. The same phenotype may be caused by alleles at different genetic loci.