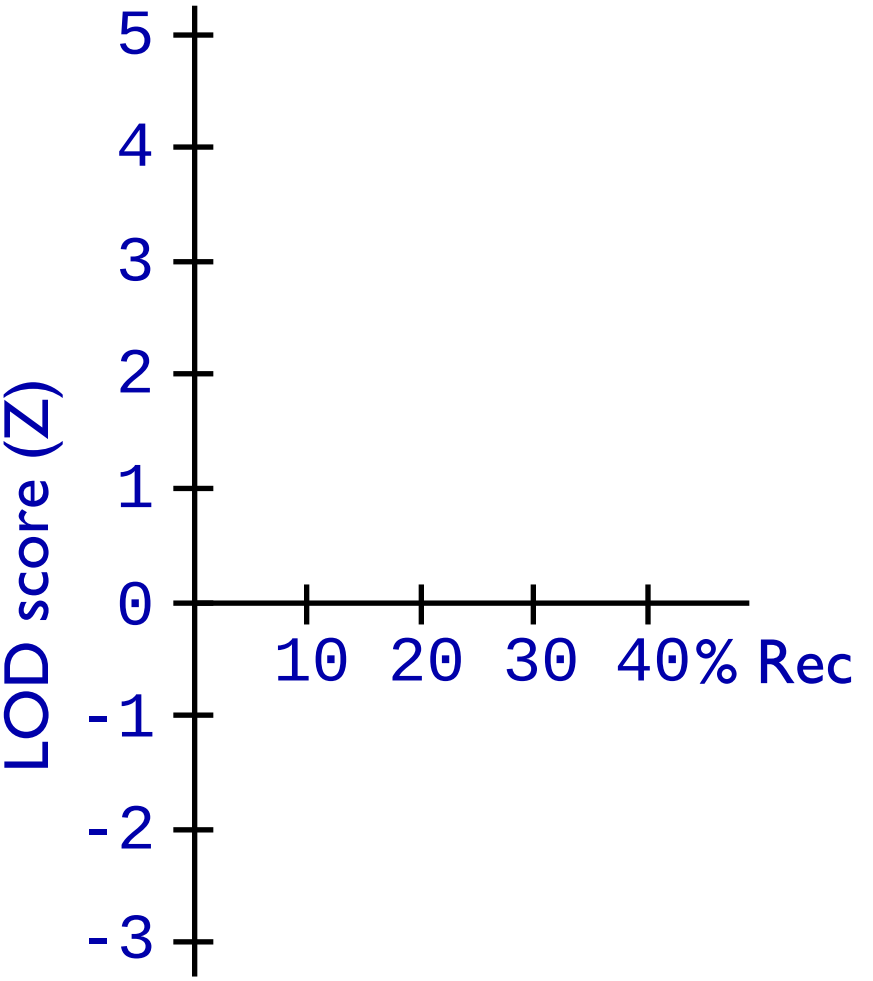
Computing LOD scores –

- Take a pairwise combination of disease gene and a polymorphic locus…
- Ask:
  - ◇ What's the probability of getting this pedigree if the two loci are **linked**…
  - ◇ What's the probability of getting this pedigree if the two loci are **unlinked**?
- Calculate LOD score
- Repeat

A hypothetical example –



Lod score of 3 = 95% probability of linkage at the proposed recombination frequency

From Lod scores – sites with highest probability of linkage to the gene

Lod scores from different pedigrees can be **added up**!
Why?

Linkage to marker sites – can be starting point for cloning the gene… **Positional cloning**

Not trivial – 1–2 cM…still ~1–2 million bp to search!

Approaches to cloning the gene

- "brute force"

- **Candidate gene** approach

- **rescue** of disease phenotype in a model system

Other applications of polymorphic site mapping technology

- **Diagnostics**

- **DNA profiling/genetic fingerprinting**

  Tabulate allele frequencies for various polymorphic sites – e.g.,

  Polymorphic site 1: 20 alleles (21-40 repeats), equal frequencies

  Polymorphic site 2: 30-40 repeats:

i.	0.15	(30 repeats)	vii.	0.05	(36 repeats)
ii.	0.12	(31 repeats)	viii.	0.10	(37 repeats)
iii.	0.08	(32 repeats)	ix.	0.09	(38 repeats)
iv.	0.09	(33 repeats)	x.	0.13	(39 repeats)
v.	0.06	(34 repeats)	xi.	0.08	(40 repeats)
vi.	0.07	(35 repeats)	xii.	0.08	(all others)

What is the probability of a person having alleles ii and iv of polymorphic site 1, and alleles v and ix of polymorphic site 2?

Some applications of DNA profiling

- Forensics

- Paternity

- Conservation biology