For classrooms

Lesson: how to read a pedigree, and where the textbook rule breaks

Biology · Genetics · Mathematics · Age 13+ · Intermediate

A free genetics lesson on pedigree analysis. Three clean family trees teach the three inheritance patterns; the fourth is real, and the rule the class just learned gives the wrong answer on it.

Free to read, use and adapt. No account, nothing to buy, nothing collected from anyone.

Full lesson, figures and updates: https://www.mygenelog.com/updates/lesson-reading-a-pedigree

What this is. A ready-to-run lesson on pedigree analysis, free to use and adapt in any school, college or university. Nothing to buy from us, no account, no data collected from anyone.

- Level: works from about age 13 through first-year undergraduate. Everyone does the same four pedigrees; the questions at the end are graded.
- Time: 45–60 minutes. The four pedigrees take twenty.
- You need: this page on a screen, or the four diagrams printed. No equipment, no consumables.
- It covers: pedigree notation, autosomal recessive, autosomal dominant and X-linked recessive signatures, why consanguinity matters for rare recessives, penetrance, and the difference between a family drawn from symptoms and the same family drawn from genotypes.

Start here: the experiment nobody could run

Mendel could do the experiment. He chose the crosses, he made them on purpose, and he counted tens of thousands of pea plants until the ratios were unarguable.

Human genetics could do none of that. You cannot cross people, you cannot choose their partners, and you get about four offspring per generation instead of hundreds. For most of the nineteenth century that looked like a permanent obstacle.

The way round it was not a better microscope. It was a drawing.

1902: a doctor draws families

Archibald Garrod was studying alkaptonuria — a condition whose most obvious sign is that urine turns black on standing. It is rare, it runs in families, and it was not understood.

Garrod could not experiment. So he collected: every published case he could find, and letters from the doctors who had reported them. He assembled 40 recorded cases. And rather than looking at the patients, he looked at their parents.

> “...of four British families in which were 11 congenitally alkaptonuric members no less than three were the offspring of marriages of first cousins who did not themselves exhibit this anomaly.”

He went looking for more, and the pattern held. His table of parentage covered 19 of the 40 recorded cases, and the same thing kept appearing: the parents were cousins, and the parents were fine.

William Bateson, reading this, recognised what it was. If a character is recessive and rare, two copies almost never meet — unless the two people carrying them are related:

> “In the case of a rare recessive characteristic we may easily imagine that many generations may pass before the union of two recessive gametes takes place... first cousins will frequently be the bearers of similar gametes, which may in such unions meet each other.”

That is the whole idea. Garrod had no experiment, no gene, no DNA — the structure was fifty years away. He had a drawing of who was related to whom, and it was enough to identify the first human trait shown to follow Mendel’s rules.

The drawing is called a pedigree, and your class is about to read four of them.

How to read one

male, unaffected

female, unaffected

affected

known carrier

genotype unknown

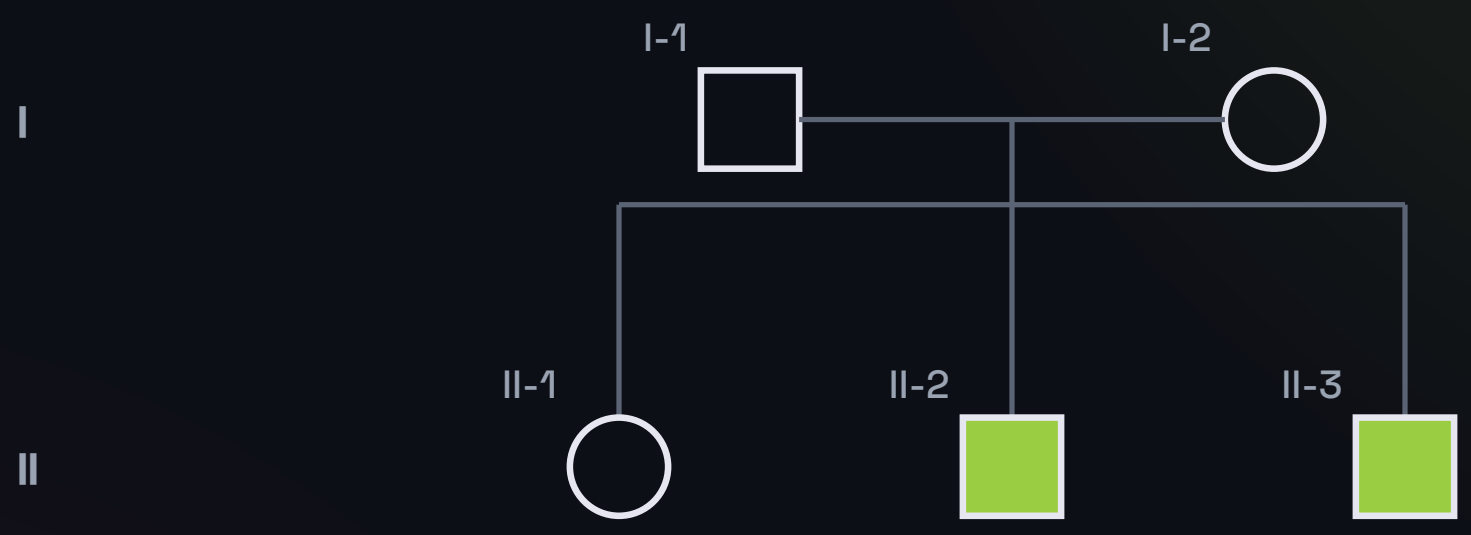
a mating

Generations are numbered with Roman numerals, individuals left to right within each.

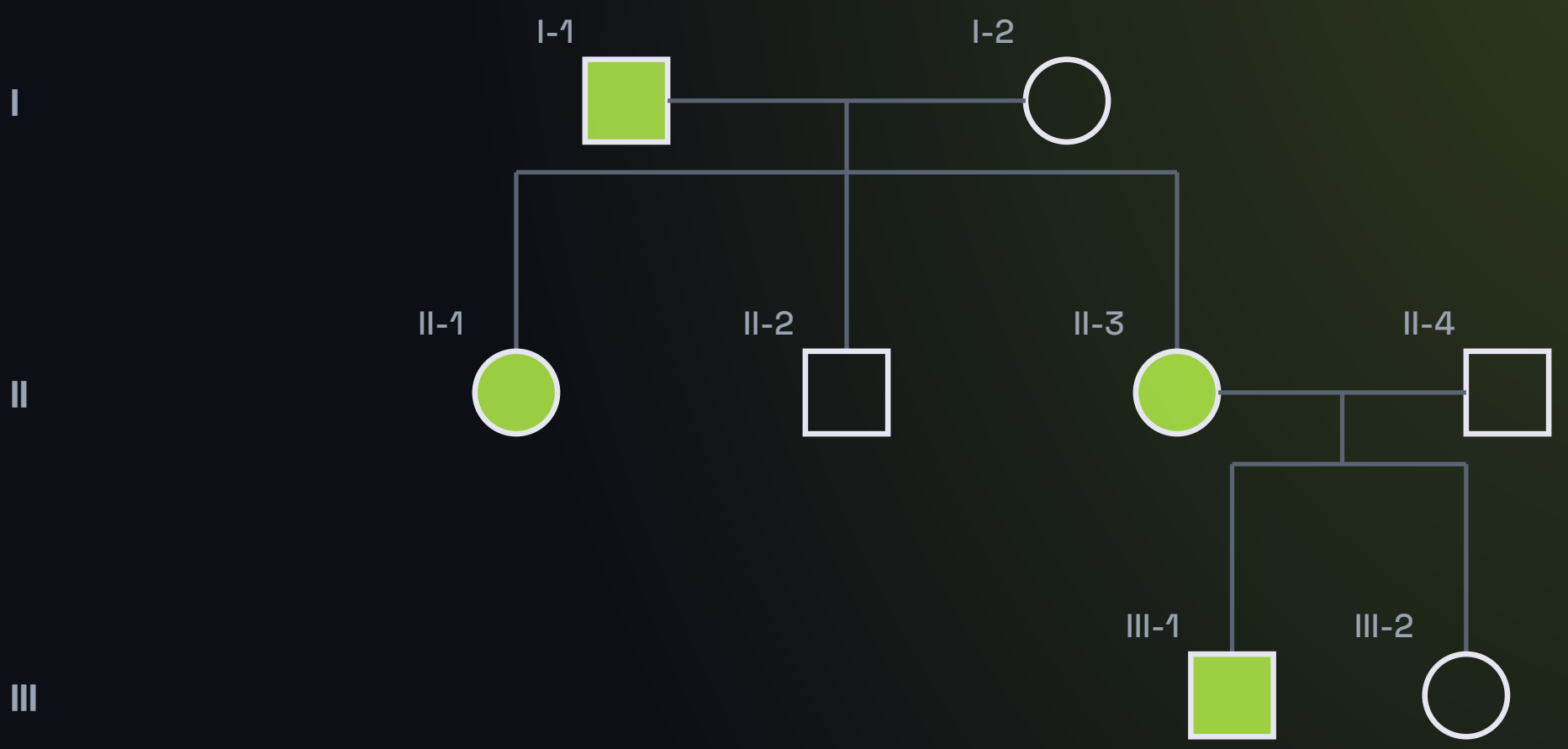
Standard pedigree notation. It is the same in every genetics textbook and every clinic, which is why it is worth twenty seconds of learning: a diagram drawn this way can be read by anyone.

The three signatures

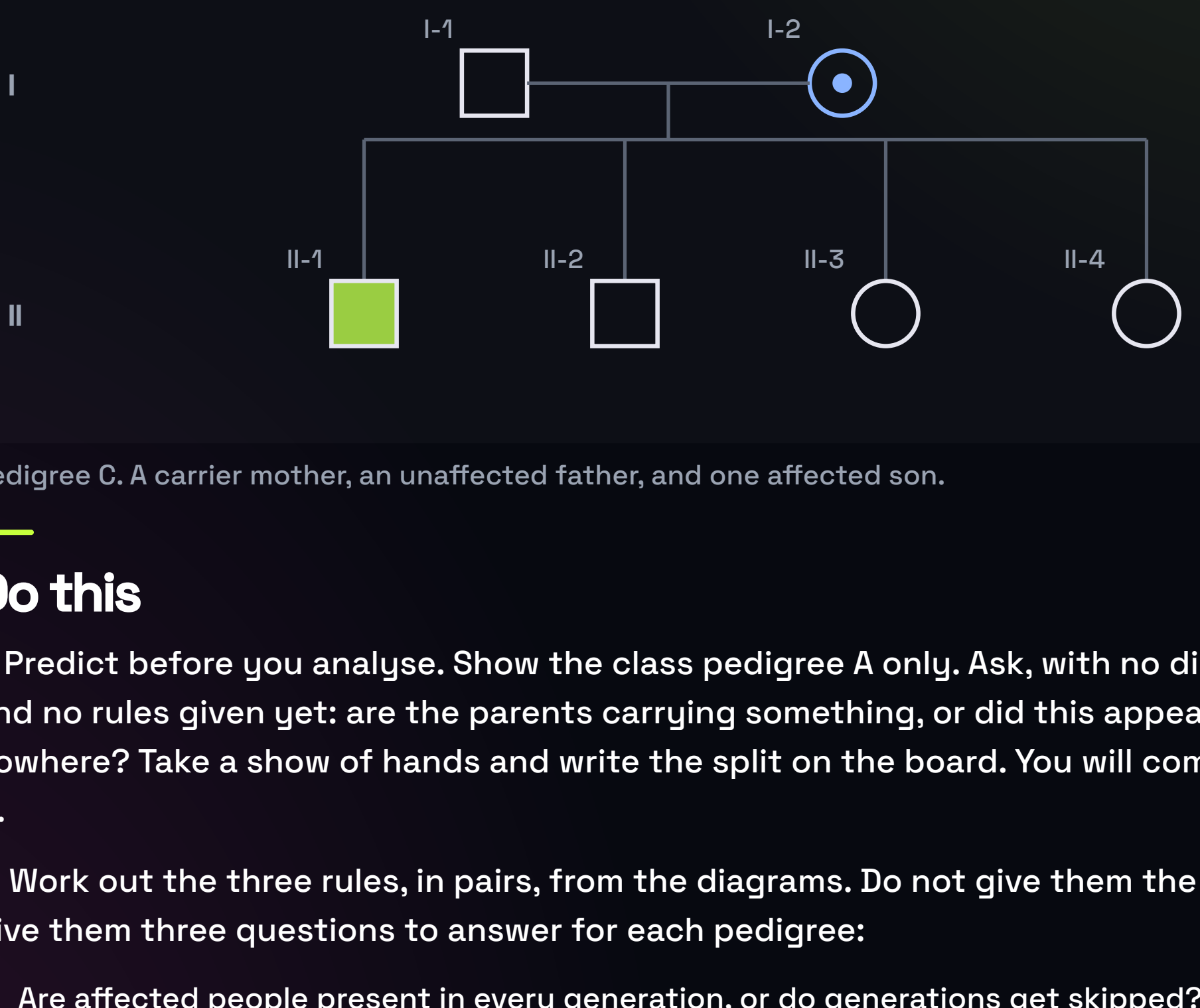
Almost every single-gene pattern a school course covers is one of three. Each leaves a different fingerprint on a family.



Pedigree A. Two unaffected parents; two of three children affected.



Pedigree B. Affected individuals in all three generations.



Pedigree C. A carrier mother, an unaffected father, and one affected son.

Do this

1. Predict before you analyse. Show the class pedigree A only. Ask, with no discussion and no rules given yet: are the parents carrying something, or did this appear from nowhere? Take a show of hands and write the split on the board. You will come back to it.

2. Work out the three rules, in pairs, from the diagrams. Do not give them the rules. Give them three questions to answer for each pedigree:

- Are affected people present in every generation, or do generations get skipped?
- Do affected parents have affected children, or do unaffected parents have them?

- Are the affected people mostly one sex?

Ten minutes. Then collect the answers on the board as a table, three pedigrees across the top and the three questions down the side. The table is the lesson: the rules fall out of it without anyone reciting them.

3. Name them. A is autosomal recessive: it skips, unaffected parents have affected children, either sex. B is autosomal dominant: no skipping, an affected parent in every affected child's line, either sex. C is X-linked recessive: affected males, unaffected carrier mothers, and — the detail worth pausing on — never father to son, because a father gives his son a Y.

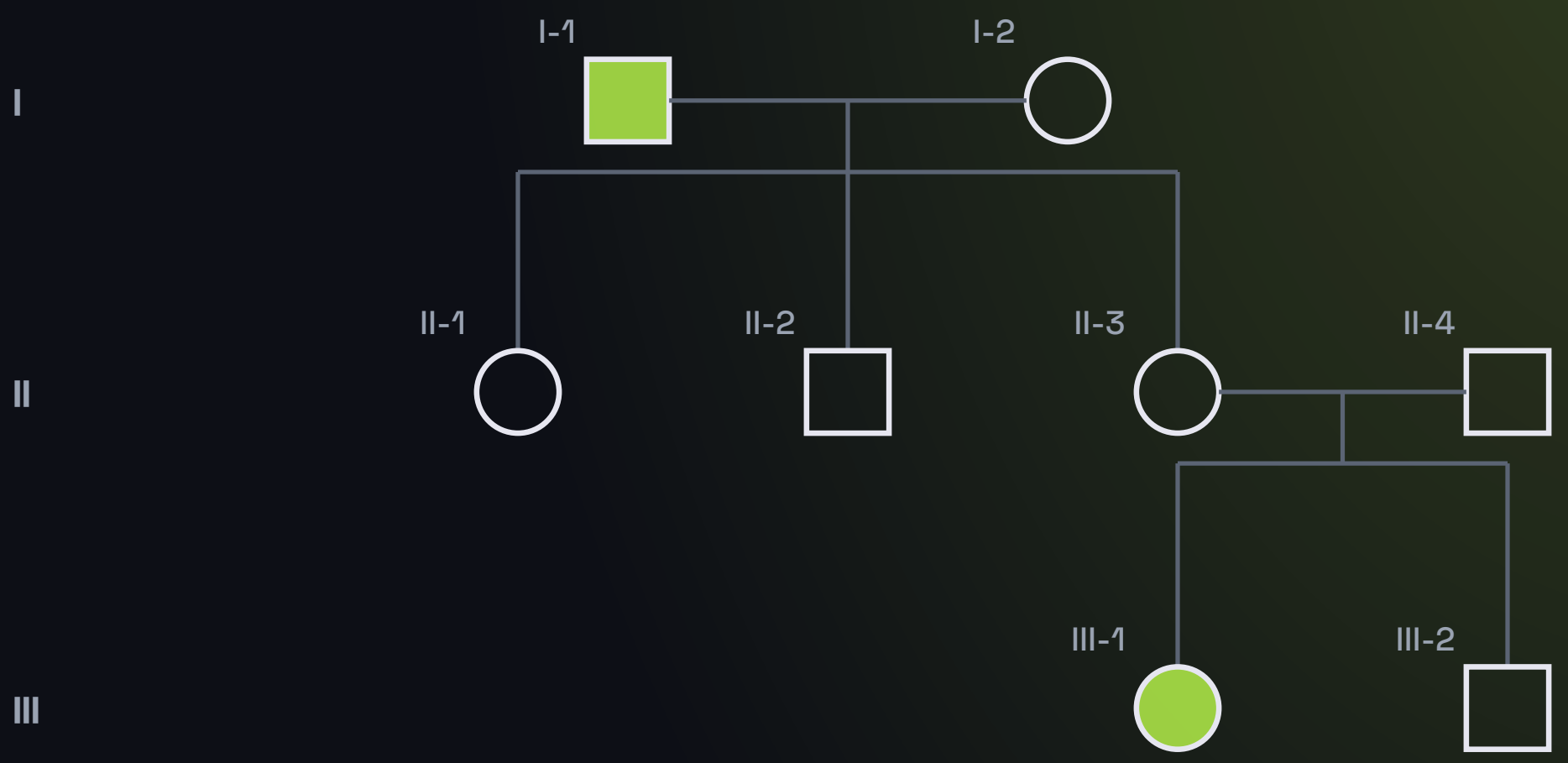
4. The control question. Ask whether pedigree A could also be X-linked recessive. Look at it again: both affected children are male, and the mother could be a carrier. With only these six people, it could. Nothing in that drawing rules it out.

This is the honest limit of the method and it is worth more than the three rules. A pedigree does not prove an inheritance pattern; it is consistent with one or more. Small families are consistent with almost anything. Garrod needed 40 cases, not one family.

Before you go any further — a rule for this lesson. Do not ask students about illnesses in their own families, and do not let the class build a pedigree of anybody in the room.

A family history is medical information about people who are not present and have not agreed to anything, and a student who discovers something about their own family in front of thirty classmates cannot take it back. Every diagram here is invented for teaching. Keep it that way — the lesson works completely without a single real family in the room.

Now the fourth one



Grandfather affected. Nobody in generation II affected. A granddaughter affected.

Pedigree D. A real inheritance pattern, drawn the way a clinic would see it.

Give the class pedigree D and the three rules they just derived. Most will reach the same answer within a minute: the trait skips a generation, so it must be recessive.

It is not. This is the shape of factor V Leiden thrombophilia, and factor V Leiden is autosomal dominant. Every person in generation II who lies between the affected grandfather and the affected granddaughter is carrying one copy. Not one of them has had a clot.

The word for what went wrong

Penetrance is the fraction of people carrying a genotype who actually show the trait. The textbook rules assume it is 100%. Almost nothing in a real clinic is.

Two conditions on this site, with the real numbers:

Condition	How common the genotype is	How often it shows
Factor V Leiden (dominant)	3–8% of people of European ancestry carry one copy — up to 10–15% in parts of southern Sweden and Greece. About 1 in 5,000 carry two.	Most carriers never have a clot in their lives.

Condition	How common the genotype is	How often it shows
Hereditary haemochromatosis (recessive)	Roughly 1 in 200 to 1 in 500 people of European ancestry are homozygous; about 1 in 9 carry a single copy.	Clinical disease develops in only a minority of homozygotes.

Read the second row again against pedigree A. A textbook recessive pedigree fills in every homozygote as affected. In haemochromatosis, most homozygotes are not. Draw that family from symptoms and you get one diagram; draw it from genotypes and you get a different one. Same family, same DNA, two drawings.

Which means the rules are not wrong, exactly. They are rules about genotypes, being applied to a drawing made of symptoms.

The argument that is still open

Here is a question with no settled answer, and your class has everything they need to argue about it.

Most people homozygous for the common haemochromatosis variant never develop iron overload. Are they patients?

If yes: they should be found and monitored, which means screening populations for a genotype that will not harm most of the people it identifies. If no: then a genotype that causes serious disease in a minority is not, on its own, a diagnosis — and we have to decide what to tell somebody who has it.

This is not a school exercise with a hidden answer. It is a live question about screening programmes, and every answer costs something.

Questions

Warm up

1. In pedigree C, why can we be certain the affected son did not get the variant from his father?
2. In pedigree A, what are the parents' genotypes? Use A for the common version and a for the rare one.
3. Why did Garrod look at the patients' parents rather than at the patients?

Core

1. The two parents in pedigree A have a fourth child. What is the probability that this child is affected? What are you assuming about penetrance to give that answer?
2. Explain, in your own words, why a rare recessive condition shows up disproportionately among the children of first cousins. Would the same be true of a rare dominant condition?

3. Pedigree D looks recessive and is dominant. Write down one thing you could measure or ask for that would settle it — and say why the pedigree alone cannot.
4. A textbook says a condition is “autosomal dominant”. A student says that means every carrier is affected. What is wrong with that, and what would you say instead?

To stretch

1. Roughly 1 in 9 people of European ancestry carry one copy of the haemochromatosis variant. Using that carrier frequency, estimate how often two carriers would have children together by chance. Compare your estimate with the observed frequency of homozygotes, about 1 in 200 to 1 in 500. What might explain a difference in either direction?
2. Garrod had 40 cases. Suppose he had found only the one family. Which of his conclusions would still have been available to him, and which would not?
3. Design a rule for when a genotype should be called a diagnosis. Test your rule against factor V Leiden, against haemochromatosis, and against a condition where every carrier is affected. Does one rule handle all three?
4. Pedigrees are drawn from what families report. Name two ways that a family’s own report could be systematically wrong, and say for each whether it would make a condition look more dominant or more recessive than it is.

Notes for whoever is teaching — where these questions are going

1. A father passes a Y to a son, so no X-linked variant of his can reach him. This single fact does more diagnostic work than any other in pedigree analysis, and students remember it because it is mechanical rather than statistical.

2. Both Aa. Watch for students who write aa for a parent because the children are affected — the parents are unaffected, which is the constraint.

3. Because the parents are where the information is. The patients tell you the condition exists; the parents tell you how it travelled. This is the move that turned a case series into genetics.

4. One quarter, and the assumption is complete penetrance — that every aa child shows it. The second half of the question is the point of the whole lesson; accept “1/4 of children are aa, and some fraction of those are affected” as the stronger answer.

5. Cousins share recent ancestors, so they are far more likely than two strangers to carry the same rare allele. It would not be true of a dominant condition: one copy is enough, so nothing has to meet anything, and cousin marriage does not raise the risk.

6. Genotype the middle generation — or look for the biochemical phenotype,

which for factor V Leiden is resistance to activated protein C. The pedigree cannot settle it because it records who fell ill, not who carries the variant.

7. Dominant describes how the allele behaves when it is expressed, not how often it is expressed. “One copy is enough to cause it in those who develop it” is a good student answer.

8. Under random mating, two carriers pair about $(1/9)^2 \approx 1$ in 81 of the time, and one quarter of their children would be homozygous — roughly 1 in 324, which lands inside the observed 1 in 200 to 1 in 500. That agreement is worth pointing at: a Hardy–Weinberg estimate made on the back of an envelope matches a measured population frequency. Good students will note that non-random mating, ancestry differences within “European”, and the fact that the observed figure is a range rather than a number all sit inside that comparison.

9. He would still have had a rare familial condition and a consanguineous marriage. He would not have had a pattern — one family is an anecdote, and the sex ratio, the recurrence in siblings and the cousin excess all require the series. This is where to make the point that sample size is not a statistical formality.

10. No single rule survives all three, and finding that out is the outcome. Push on any rule that quietly requires knowing the future.

11. Undiagnosed or misdiagnosed relatives, and relatives who died before the age of onset, both make a condition look more recessive by hiding affected carriers. Selective recall — families remember the dramatic cases — can push the other way. Adoption, non-paternity and small family size are all acceptable answers.

Take it further

- Factor V Leiden — the real pedigree D: what the variant does to a clotting protein, and why most carriers never know.
- Hereditary haemochromatosis — the recessive with the low penetrance, and the screening argument in full.
- ABO blood group — a codominant trait with three alleles, which is the natural next pedigree to try.
- Lesson: the PTC taste test — the companion lesson, where the textbook’s one-gene-two-alleles story turns out to be a haplotype.

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