Oxford Handbook of Clinical Diagnosis

Third edition

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Chapter 1

The diagnostic process

The purpose of this book

This book explains how to interpret symptoms, physical signs and test results during the diagnostic process. There are many books that provide lists of differential diagnoses. However, this one also explains how you should use these lists. Each section describes:

- The main differential diagnoses of a single diagnostic 'lead'
- How to 'differentiate' between these differential diagnoses
- How to confirm the diagnosis and also to 'finalize' it using the outcome of treatment (see ➔ 'Transparent' reasoning, p.5, ➔ Changing diagnostic leads, p.7 and ➔ Confirming and finalizing a diagnosis, p.8).

Making diagnostic reasoning and decisions transparent

The book explains how to outline your diagnostic reasoning on paper. It does this by showing you how to write a list of differential diagnoses and established diagnoses, each with its supportive evidence so far, which includes the result of management (see ➔ An evidence-based diagnosis and plan, p.13). This can be used in a draft management plan and later in a hospital hand-over or in a discharge summary. The differential diagnoses in the sections of this book, with their evidence and initial management, are described in the same format and can be used as example entries when writing out an outline of the diagnoses and evidence, which includes the result of the management for a patient.

Understanding the reasoning of others

This book helps you to understand the diagnostic reasoning and decisions of others. In order to do so, you (and patients, carers, nurses, and other health professionals) have to ask:

- What is the current management plan (the pieces of advice, treatments, tests, and follow-up arrangements)?
- For each of these items, what are the diagnoses (provisional, probable, definitive, and final)?
- What is the evidence for each diagnosis (how it presented, how it was confirmed, and its markers of progress or outcome)?

Look up the 'problem findings' and diagnoses in this book so that you know what type of answers to expect to these questions. You can write them out in a similar format (see ➔ An evidence-based diagnosis and plan, p.13). After hearing these answers, you may wish to make your own notes in response.

Checking a clinical impression and explicit reasoning

It is important to check all diagnoses and decisions. Reasoning alone using knowledge from a book of this kind is not enough. Such reasoning should be checked by discussing it with someone who is familiar with the situation from past experience and who can recognize if the reasoning makes sense. However, it is equally important to check that diagnoses and decisions made 'intuitively' make sense when compared with transparent reasoning of the type described in this book.

When and how to use this book

This book can be used:

- When assessing a patient, e.g. after the history of presenting complaint, after completing the full history, after completing the examination, and when the test results come back
- In the same way during problem-based learning with case histories
- During private study and revision to allow you to solve clinical problems later without having to refer to the book
- When asking someone else to explain a diagnosis and decision to you.

If the presenting complaint is severe (e.g. pain or breathlessness), disabling (e.g. inability to move a limb or speak), or unusual (e.g. coughing or vomiting blood), then it will tend to be good lead with a shorter differential diagnosis. The most useful diagnostic leads are described in this book—look at the 'Contents' list of each section so that you can recognize them.

Remember that many symptoms and other findings are due to self-limiting conditions that are transient or are corrected within hours or days by the body's own restorative mechanisms. Such self-limiting conditions always have to be considered as part of any differential diagnosis. If the finding is mild and has only been present for a short time and is not accompanied by other features, then it is more probable that it will resolve spontaneously without its cause being identified. However, it is important to review such patients to ensure that there is improvement or resolution, by asking the patient to return if the problem persists. The ability to deal with such self-limiting conditions is a very important skill that has to be learnt by experience. Severe and persistent findings will often turn out to have a cause that requires medical attention.

If the presenting complaint is not a good lead but has a long differential diagnosis, then consider what systems (e.g. cardiovascular or respiratory) it came from and ask 'direct questions' directed at this system to try to find better leads. Also, focus on that system first in your examination. Note the speed of onset; this will suggest the underlying disease process. Onset within seconds suggests an 'electrical' cause, e.g. a fit or rhythm abnormality; onset over seconds to minutes suggests an embolus, a trauma, or rupture; onset over minutes to hours suggests a thrombotic process, over hours to days an acute infection, over days to weeks a chronic infection, weeks to months a tumour, and months to years a degenerative process.

Read this book during private study or revision by covering the column of diagnoses on the left side of the table and testing your ability to recognize the diagnoses when you read the nature of the diagnostic lead associated with the table, and the suggestive and confirmatory findings on the right side of the table. If you are able to do this successfully, you will soon learn to take a history and examine a patient without having to use this book. Do it first with the symptoms and physical signs that are common in your current (and next) clinical attachment so that you are prepared.

‘Intuitive’ reasoning

Most of the time, experienced doctors use a non-transparent reasoning process. This seems to involve recognizing combinations or patterns of findings consciously or subconsciously, which suggest or confirm a diagnosis, or indicate that some treatment should be given. This is a skill that is improved by repetition. This book will encourage you to do this sooner. However, all doctors specialize and the information in this book will be of help to experienced doctors with patients outside their specialty.

If you were told that a patient had suffered sudden onset of sharp chest pain over seconds to minutes, then this ‘diagnostic lead’ will make you think consciously or subconsciously of a pneumothorax, pulmonary infarction, etc. If another patient has suddenly started coughing up blood, then this lead would suggest acute bronchitis, pulmonary infarction, bronchial carcinoma, pulmonary tuberculosis, etc. However, if both happened in the same patient, your mental links would ‘intersect’ on pulmonary infarction and it would surface to consciousness.

If you were to come across this combination of features and had read in this book during private study that they ‘suggested’ pulmonary infarction, then you might think of this diagnosis directly. If you came across these findings many times and a diagnosis of pulmonary infarction was usually confirmed on CT-pulmonary angiogram, then you would soon recognize that the combination of findings as suggesting pulmonary infarction (like recognizing someone’s face). The psychological process that leads to such recognition is sometimes described as ‘Gestalt’ (German for an overall impression). Instead of writing ‘diagnosis’ many doctors will write ‘Impression:’ to indicate this.

If the findings so far do not point to a single diagnosis with certainty, then you will have to consider a number of other possibilities. It may then be reasonably certain that the diagnosis will turn out to be one of these. A device for doing this is not to specify a list of diagnostic possibilities, but to write down a term that represents a group of diagnoses, e.g. ‘pulmonary lesion’ or ‘autoimmune process’.

If a diagnosis or small number of differential diagnoses do not come to mind readily in one of these ways, then it is important to turn to the ‘transparent’ reasoning process. You will always come across unfamiliar situations however experienced you become, so the ‘transparent’ approach will always be important.

'Transparent' reasoning

Diagnostic reasoning is transparent if the findings used to arrive at a diagnosis are specified clearly and if the interventions resulting from that diagnosis are also specified. The combination of findings used might have been recognized by the diagnostician at the outset. However, in many cases, the combination of findings would have been assembled by a reasoning process of elimination (see Diagnostic leads and differentiators, p.6).

A diagnosis will only be certain or 'definite' if the findings so far are 'sufficient' or 'definitive' by an agreed convention. For example, two fasting blood sugars of at least 7mmol/L on different days by convention provide a 'sufficient' criterion for confirming diabetes mellitus. There are other 'sufficient' criteria, e.g. two random sugars over 11mmol/L. All the different sufficient criteria collectively make up the 'definitive' criteria. This means that it is 'necessary' to have at least one of these various criteria. At least one fasting glucose of at least 7mmol/L is also 'necessary' (but not 'sufficient') to confirm the diagnosis, so if the first of a pair of fasting blood sugars is below 7mmol/L, the diagnosis is logically 'eliminated' because they both can no longer be over 7mmol/L.

If the first of two fasting sugars is 7.1mmol/L, then this makes diabetes mellitus more probable than not. The differential diagnosis will also include 'impaired fasting glucose' (if the next result is less than 7mmol/L). Medical conditions change and even though a diagnosis is 'eliminated', any borderline tests may be repeated quite soon. In reality, few diagnoses are defined precisely in this way and a doctor may 'confirm' a diagnosis if the probability of benefit from its advice or treatment is judged to be high and cite in a transparent way the findings on which this confirmation is based.

'Over-diagnosis' is said to occur if patients are labelled with a diagnosis when a high proportion show little prospect of benefiting from any advice or treatment directed at that diagnosis. For example, 'diabetic albuminuria' is said to be present if the urinary albumin excretion rate (AER) is between 20 and 200 micrograms/min on at least two out of three collections, provided that other findings indicate that there is no other cause of albuminuria present. However, there is no difference in those developing diabetic nephropathy within 2 years between those taking placebo or active treatment for the 1/3 of patients with an AER between 20 and 40 micrograms/min, suggesting that there is 'over-diagnosis' as this group of patients do not benefit. Diagnostic criteria need to be based closely on treatment outcomes to avoid this.

A diagnosis becomes final when all the findings that led to the diagnosis being considered can be 'explained' by that diagnosis. For example, if a patient complained of persistent fatigue and this did not respond to the treatments and advice for diabetes, then an additional diagnosis has to be considered. The diagnosis of diabetes mellitus may have been confirmed definitively, but the diagnostic process will not be finalized until other reasons for the fatigue have been confirmed or excluded. It is only then that the process stops. The 'final diagnosis' is then a 'theory' and no longer a hypothesis to be tested further, at least for the time being.

Diagnostic leads and differentiators

A combination of features that identifies a group of patients within which the frequency of those with a diagnosis is high (or even 100%) might well be recognized at the outset. If not, a combination of findings can be assembled 'logically' by using reasoning by elimination. This would be done by first considering the possible causes of a single finding, called a 'diagnostic lead' (e.g. localized right lower quadrant abdominal pain). The possible diagnostic explanations for this 'lead' are then considered, one is chosen (e.g. appendicitis) and findings looked for that occur commonly in that chosen possibility and less commonly (ideally rarely or never) in at least one other possibility.

If a finding (e.g. being male) occurs often in a diagnosis being pursued (e.g. appendicitis) but cannot happen in a differential diagnosis (e.g. ectopic pregnancy), then that diagnosis can be ruled out, being female being a 'necessary' condition for suffering an ectopic pregnancy! However, if a finding such as guarding occurs commonly in the diagnosis being chased (e.g. appendicitis) and less frequently in another diagnosis (e.g. non-specific abdominal pain—NSAP) then NSAP will become less probable, not ruled out.

The 'lead' and the new finding will form a combination within which the frequency of the diagnosis being chased (e.g. appendicitis) becomes more frequent and the diagnosis in which the finding occurs less often becomes less frequent in that combination of findings.

The frequency with which a finding occurs in a diagnosis is often described as its 'sensitivity' by epidemiologists, i.e. the frequency with which the finding 'detects' the diagnosis when screening a population. Statisticians also call the 'sensitivity' the 'likelihood' of the finding being discovered when the patient is known to have the diagnosis. If the finding is 'likely' to occur in a diagnosis being chased and is 'unlikely' to occur in one of its differential diagnoses, then the ratio of the two likelihoods represents the finding's ability to differentiate between those two diagnoses. This makes one more probable and the other less probable. This book describes such findings under the headings of 'Suggested by' and 'Confirmed by'. It is findings that cannot occur by definition in other diagnoses that 'confirm' a diagnosis—'definitely'.

Eddy and Clanton analysed the thought processes of senior doctors participating in the Clinico-Pathological Conferences at the Massachusetts General Hospital[1]. They pointed out that choosing a diagnostic lead, e.g. localized right lower quadrant abdominal pain (which they called a 'pivot') was central to these experienced doctors' explanations when solving diagnostic problems. They also noted that during diagnostic reasoning, other findings (e.g. guarding) were used to 'prune' some of the differential diagnoses (e.g. pruning away NSAP).

There has been a re-awakening of interest in all this as 'stratified' or 'personalized' medical research. The aim is to have more differential diagnostic sub-divisions so that each predicts treatment response more accurately.

Changing diagnostic leads

A patient presenting with breathlessness will have a long list of differential diagnoses. A diagnostician might suspect a 'cardiac' or 'respiratory' reason and after asking for cardiovascular and respiratory symptoms and looking for physical signs, might ask for a chest X-ray (CXR) in the hope of getting a better diagnostic lead. A circular shadow on a CXR will have a much shorter list of differential diagnoses and a CT scan showing a lesion contiguous with a bronchus an even shorter one. A biopsy might provide a diagnostic criterion for a bronchial carcinoma. However, this may only be a working diagnosis even if it is confirmed or definite. All the diagnoses applicable to that patient will not become final until the patient's symptoms have been cured, stabilized, or predicted correctly and no follow-up or other action needs to be taken.

If we come across a powerful finding or combination of findings (e.g. a dense, round shadow on a CXR), this will form a stronger lead with a shorter list of differential diagnoses. It is easier to make a fresh start with such a powerful new finding than to try to work out which of a long list of original diagnostic possibilities (e.g. breathlessness) are being made more probable or less probable by the new finding. Therefore, another measure of a powerful finding is the number of differential diagnoses required to explain, say 99% of patients with that finding. The better the lead, the fewer the differential diagnoses.

Care has to be taken to consider spurious and self-limiting causes for any lead (e.g. a CXR appearance), especially if the differential diagnoses of that lead finding cannot explain any of the patient's symptoms. The same consideration applies when a screening test is performed, e.g. a mammogram. If the patient is asymptomatic, then it is important to consider the possibility that a new finding might be due to a self-limiting condition that might resolve spontaneously without medical assistance. One option would be to repeat the test after a short interval to see if there has been regression. Asymptomatic conditions that are detected incidentally are often labelled wrily as 'incidentalomas'. In many cases they are investigated aggressively and the patient sometimes subjected to potential harm (e.g. radical surgery) with adverse consequences only to find out that the lesion was innocent after all. This is sometimes described as 'over-diagnosis' and 'over-treatment'.

Confirming and finalizing a diagnosis

A diagnosis can be confirmed in different ways. The different confirming (or 'sufficient') criteria taken together form the 'definitive criteria' of the diagnosis. The definitive criteria thus identify all those and only those with the diagnosis. Such criteria can be based on symptoms, signs, and test results (and, in some cases, on the initial result of treatment). However, few patients with a diagnosis will require all the advice or treatments suggested by that diagnosis (e.g. not all patients with diabetes mellitus will need insulin). Further findings may have to be looked for called 'treatment indications', which often form sub-diagnoses. For example, the presence of a very high blood sugar, weight loss, and persistent ketones in the urine would be one such 'indication' for giving insulin; that patient might also be diagnosed as having 'Type 1 Diabetes Mellitus or Type 2 Diabetes Mellitus with severe insulin deficiency'.

In many cases, a diagnostician will start treatment when a diagnosis is probable or suspected without waiting for formal criteria to be fulfilled (e.g. a treatment given on suspicion of meningitis). In such a situation, the diagnostician might imagine the existence of a large number of identical patients who were randomized into different treatment limbs of a randomized clinical trial. The treatment chosen would be the one 'imagined' (i.e. 'predicted', ideally with a known track record of success) to produce the best outcome, bearing in mind the benefits and adverse effects. If the patient improves on treatment, then this may also be regarded as confirmation of the diagnosis, if patients with no other diagnosis could have improved in that way. However, if the patient and diagnostician were satisfied that nothing else needed to be done, then the diagnosis would become 'final'. This could happen even if the diagnosis was only probable, e.g. if a severe headache had been suspected of being meningitis, had resolved on antibiotics but no bacteria had grown in the laboratory, then the final diagnosis would be 'probable bacterial meningitis'.

There may be no formal criteria that are suitable for use in day-to-day clinical care. One approach is to provide a trial of therapy, and if the patient improves, to regard this as a confirmatory result and no other explanation is looked for. The confirmatory findings in this book are based on all of the approaches outlined here. They reflect typical approaches used in the authors' experience. However, none of these approaches are ideal; future medical research may improve matters.

Some patients with a diagnosis have mild conditions so that treatment is not necessary; others may be so severe that it is too late to treat, while others are treatable—this subdivision is known as 'triage' in emergency settings. The group with a diagnosis may also contain subgroups with causes and complications that also require treatment. Therefore, diagnoses (probable or confirmed) may be thought as 'envelopes' that enclose subgroups of patients with other diagnoses for which different actions are indicated. The way in which evidence can be sought to form diagnostic indications and sub-diagnoses is described in Chapter 13.

Evidence that 'suggests' a diagnosis

It is important to remember what 'evidence' means. Evidence is made up of facts, which are records of observations and actions that took place at a place and time. A 'fact' becomes 'evidence' when it is used to make a prediction—in the context of this book, about the presence of a diagnosis (which leads to other predictions that include what could be done to improve matters). A diagnosis is the title to what we picture or predict is happening now, has happened in the past, and what will happen to a patient in the future. This will include causes and complications of the diagnosis. Some of this may be pictured with certainty (i.e. what has been observed already) or with different degrees of probability, depending on the available evidence.

Evidence may be based on facts such as symptoms, signs, and test results recorded in a particular patient. This is 'particular' evidence from a particular patient, which is a 'particular' proposition in logic. In contrast to this, 'general' evidence will be based on facts related to groups of patients such as the result of a clinical trial, which is a 'general' proposition in logic. In order to practice evidence-based medicine, we have to relate the 'particular' evidence from a particular patient to 'general' evidence about groups of similar patients that we have observed and documented carefully or published by others in the medical literature.

The predictions based on 'particular' evidence are diagnoses with different degrees of probability about what is wrong with a patient and what to do. If the listener is going to accept such an opinion on the basis of the evidence, there has to be agreement as to what is acceptable as evidence, which includes how the evidence was obtained. This book contains typical evidence that is used to 'suggest' probable diagnoses and to 'confirm' diagnoses according to definitive criteria that are accepted at present by most doctors in their day-to-day work. These conventions will no doubt change as more 'general' scientific evidence is published.

Each differential diagnosis in every section is followed by the evidence that 'suggests' the probable presence of the diagnosis. The diagnosis is considered to be 'definite' when the confirmatory 'sufficient' criteria are present. In each section, the confirmatory evidence for each diagnosis is provided under another subheading.

For example, localized right lower quadrant abdominal pain with guarding 'suggests' that the diagnosis will probably be appendicitis (see ➔ Localized tenderness in left or right lower quadrant p.363). The diagnosis of appendicitis is 'confirmed' by the appearances at laparotomy and by the resulting definitive histological examination. It is important to note that not all the available findings from the patient have to be used in the reasoning process to confirm a diagnosis. The findings selected may be called the 'central' evidence'. For example, a patient with a large number of findings that includes localized right lower quadrant (LRLQ) pain and guarding can be regarded as a member of a set of such patients with LRLQ and guarding within which the frequency of appendicitis is high (see ➔ Picturing probabilities, p.618).

Confirmatory findings based on general evidence

A confirmatory finding identifies a group or set of patients that 'envelopes' all those with indications for treatment 'explained' by the diagnosis. If new treatment indications are discovered that are explained by the diagnostic theory, then 'the envelope' may need to be expanded. For example, it was discovered some years ago that many patients with features of diabetic retinopathy requiring treatment had blood sugars outside the criteria for diabetes mellitus. Because of this, the World Health Organization and the American Diabetes Association suggested that the 'envelope' for diabetes should be expanded by lowering the diagnostic cut-off point of fasting blood glucose.

It is also possible that new tests may be discovered in the future that select patients more efficiently for treatment. If these new treatable patients lie outside the diagnostic group that was previously considered for treatment, then it might be appropriate to use the new test to identify patients who should be deemed to have the diagnosis. So if 'confirmatory' tests are to be chosen in an evidence-based way, then they should be shown to be superior to rival tests by including more patients who respond to the advice or treatments directed at the diagnosis and excluding more patients with no prospect of responding.

Many diagnoses are based on test results that are 'abnormal', i.e. above or below two standard deviations of the test result in the general population. This means that the 2.5% of patients above and 2.5% of those below these two standard deviations could be regarded as 'abnormal'. The use of two standard deviations is arbitrary and not 'evidence-based'. For example, patients with diabetes mellitus are 'diagnosed' as having 'diabetic microalbuminuria' if their AER are above two standard deviations of the mean (i.e. >20 micrograms/min).

However, in a clinical trial on patients with type 2 diabetes mellitus where their blood pressures had been controlled, there was no difference between those on treatment and placebo in the proportion of patients developing nephropathy within two years if they had an AER between 20 and 40 micrograms/min. This suggests that the cut-off point should be 40 micrograms/min. However, before changing the definition, it would be important to ensure that the patients inside the envelope with an AER between 20 and 40 micrograms/min might not benefit in other ways, e.g. by some being prevented from developing peripheral or coronary artery disease.

Ruling diagnoses in and out

A diagnosis is 'ruled in' if at least one of its confirming (or sufficient) criteria is present. A diagnosis is 'ruled out' if it can be shown that the patient lies outside the diagnostic envelope by showing that one of its 'necessary' criteria is absent. Another way of doing this is to show that not one of the possible confirming (or sufficient) features is present. Another way is to show that a single necessary feature is absent, which must occur in those with the diagnosis, e.g. that the patient is not female and, therefore, cannot have an ectopic pregnancy. Such a constant diagnostic finding is called a 'necessary' criterion, of course.

Findings that suggest diagnoses based on general evidence

The best findings for 'suggesting' probable diagnoses are those which, when used alone or in combination with others, predict the presence of 'confirmatory' test results with the highest frequency of success. The general evidence for the ability of findings to do this during population screening is usually offered in the form of indices such as sensitivity, specificity, and likelihood ratios (the use of such indices can be misleading, however; see ➔ Things that affect 'differential' and 'overall' likelihood ratios, p.627). However, in order to assess the usefulness of tests during the differential diagnostic process, other indices have to be used. One index is the number of diagnoses required to explain most (e.g. 99%) of the differential diagnoses of a diagnostic lead—the fewer the better.

Another index is the ability of a test to differentiate between pairs of diagnoses in such a lead. If a test result occurs commonly in patients with confirmatory findings of one diagnosis and uncommonly in patients with another diagnosis, then that test will help to differentiate between them. The difference in these frequencies of occurrence can be measured by their ratio.

Statisticians describe the frequency of a finding that occurs in those known to have a diagnosis as the 'likelihood' of it occurring (the 'likelihood' is also known to epidemiologists as the 'sensitivity'). The difference between these 'likelihoods' for two different diagnoses can be represented by the ratio of the two likelihoods. As this ratio refers to a pair of differential diagnoses, we can call it a 'differential likelihood ratio'. This is different to the 'overall likelihood ratio', which is the frequency of a finding in patients with a confirmed diagnosis divided by the frequency of the same finding in *all* those confirmed *not* to have that diagnosis. This 'non-differential' or 'overall' likelihood ratio is more useful when screening populations by using one test to detect one diagnosis. The 'overall' likelihood ratio is not as helpful for differential diagnoses (see ➔ Evidence for a finding's role in reasoning by elimination, p.625 for a discussion about likelihood ratios).

Explaining a diagnostic thought process

You may well have arrived at differential diagnoses by using intuitive, non-transparent, pattern recognition and not considered in an explicit way how it was done. Alternatively, you may have recorded your team's consensus opinion. However, you may be asked by a patient, student, nurse, or doctor to explain your thinking. In fairness, the way that your own mind (let alone someone else's mind) has actually worked subconsciously may be impossible to explain.

The first step is to write a summary of the positive findings, diagnoses, evidence, and management, as shown in ➔ An evidence-based diagnosis and plan, p.13. The original evidence for established diagnoses (e.g. type 2 diabetes mellitus) may not be available. However, for new diagnoses, choose from the evidence the best lead with the shortest differential diagnosis. Use the other findings to show that the one (or some) diagnoses are more probable or confirmed, and others less probable or ruled out.

If these conclusions of the non-transparent and transparent thought processes are not the same, you may wish to revise your opinion and list of differential diagnoses. By doing this, you will be checking diagnoses by using a different mental process in the same way as you would check the answer to arithmetic addition by adding up the list of numbers in a different order.

In order to avoid overlooking diagnoses, jog your memory by using 'sieves' to use 'recognition' to and help 'recall' by listing the possible broad anatomical and physiological explanations (see ➔ Medical and surgical sieves, p.14).

An evidence-based diagnosis and plan

Positive findings summary

Central chest pain for 4h with jaw discomfort, sweating, and nausea (1/10/13). PMH of hypertension for 10y. History of mild jaundice during febrile illnesses for years. BP 146/88 on admission (1/10/13). ECG: T wave inversion S2, AvF, V4, and V5. Latest HbA1c=8.7% (5/8/13).

Assessment and plan

?Unstable angina

?Non-ST elevated myocardial infarction (NSTEMI)
Outline evidence: central chest pain for 4h with jaw discomfort, sweating and nausea (1/10/13). ECG: T wave inversion S2, AvF, V4, and V5.
Plan: for troponin I immediately and 12h after onset of pain. Aspirin 300mg stat, bisoprolol 5mg od, isosorbide mononitrate 10mg bd.

?Gilbert's disease

?Cholelithiasis
Outline evidence: jaundiced sclera, history of mild jaundice during febrile illnesses for years, none of liver disease (1/10/13).
Plan: check bilirubin, urobilinogen, AST, γGT.

Other active diagnoses

Essential hypertension
Outline evidence: history of raised BP for 10y. Current BP 146/88 on admission (1/10/13).
Plan: continue bendroflumethiazide 2.5mg od, perindopril 2mg od.

Type 2 diabetes mellitus
Outline evidence: latest HbA1c = 8.7% (5/8/13).
Plan: stop gliclazide 160mg bd. Start insulin sliding scale.

Medical and surgical sieves

Check that you have not forgotten something by using a 'medical sieve'. For example:

- Social system and environment
- Locomotor system
- Nervous system
- Cardiovascular system
- Respiratory system
- Alimentary system
- Renal and urinary tract
- Reproductive system
- Endocrine and autonomic system
- Haematological and immune system.

Consider each of these systems by using the 'surgical sieve'. Is there a problem that is congenital, infective, traumatic, neoplastic, or degenerative?

There are many such 'sieves' in use; choose the ones that appeal to you.

The information in the pages of the OHCD is also set out in the same format as the Assessment and Plan (compare diagnoses of 'unstable angina' and 'NSTEMI' with those in ➔ Chest pain—alarming and increasing over minutes to hours, p.174). The section on chest pain gives some differential diagnoses with typical suggestive and confirmatory evidence that could also be added to those in ➔ An evidence-based diagnosis and plan, p.13. You may refer to these as examples when writing your own assessments and plans.

Diagnoses, hypotheses, and theories

Although the findings used to confirm a diagnosis can be observed, all things pictured or imagined under the title of the diagnosis cannot be confirmed by observation, e.g. molecular changes in damaged tissue or what would have happened in a particular patient if a treatment had not been given. Not only does this apply to hypotheses for individual patients, it also applies to what is imagined about populations of patients in scientific hypotheses and theories. It is thus possible that something else will be imagined or pictured in future that is also compatible with findings previously explained by another theory.

This is why the philosopher of science, Karl Popper, argued that general hypotheses and theories cannot be proven or confirmed in their entirety (see also ➔ Reasoning with hypotheses, p.637). However, if a new observation is inconsistent with one aspect of the hypothesis, it will have been 'falsified'. It will thus have to be changed to some degree (perhaps completely or slightly) to take the new observation into account.

Raised ST segments on an ECG in someone with severe central chest pain were formerly part of the criteria for confirming 'myocardial infarction', which suggested that a part of the myocardium was dead. However, one aspect of this theory has been 'falsified' because it has been discovered that some (or all) of the 'infarcted' myocardium is salvageable. With our new understanding, we use the same findings to 'confirm' an 'ST elevated myocardial 'infarction'. (It would be more accurate to say 'ST elevated acute myocardial ischaemia'.) We have modified the theory and now think that the process of 'infarction' is not complete and that the 'ischaemia' can be stopped with treatment, with reversal of many changes.

However, it is important to assess the reliability of the 'falsifying' fact. This is done by estimating the probability of the 'falsifying' observation being *replicated* by other scientists (or another doctor if the hypothesis is a diagnosis about an individual patient based on particular evidence). If the probability of replication of the evidence is high about a 'general' observation, then the observation may be accepted by the scientific community (but many may go to the trouble of repeating the study to make sure). If the *P* value is low or the 95% confidence intervals are narrow, then the probability of non-replication due to chance observations alone will be low. However, before we can conclude that the probability of replication is high, we must also be satisfied that the probability of non-replication due to other reasons is low (e.g. non-replication because of the presence of contradictory results in other studies, poor or idiosyncratic methodology, dishonesty, etc.). This is discussed further in ➔ Estimating the probability of replication with reasoning by elimination, p.636.

Imagining an ideal clinical trial

The findings used to define a 'diagnostic envelope' should enclose the best treatment indication criteria. These criteria should be chosen ideally from a number of candidate criteria. The chosen treatment criterion should be the one that produces the clearest outcome difference between the treatment and control in a comparative trial when all patients with some prospect of benefit are included. For example, when method A for measuring microalbumin in urine chose patients for a trial, 15.3% developed nephropathy on placebo and 7.7% developed nephropathy on treatment, the proportion benefiting being 7.6% (NNT=13.1). However, with method B, 25.9% developed nephropathy on placebo and 11.1% developed it on treatment, the proportion benefiting being 14.8% (NNT=6.9). This would suggest that method A was not identifying patients who benefited so well and would be inferior to method B. This is discussed in detail in ➲ Analysing clinical trials to 'stratify' diagnostic and treatment criteria, p.633; ➲ How to improve treatments by better selection or 'stratification' of patients, p.634; ➲ Studies to establish treatment indication and diagnostic cut-off points, p.635.

In the absence of detailed trial data, a doctor may have to guess whether a patient's findings would identify a group of patients who would benefit from the treatment more than a placebo, bearing in mind side-effects, costs, etc. If, on balance, this would be the case, the doctor could apply a diagnostic term that would summarize his theoretical explanation as to why giving that treatment to a patient with that combination of findings would be better than not doing so.

Decision analysis

Decision analysis is a discipline that models mathematically what would happen if a detailed clinical trial were performed to compare the treatment options being considered for a particular patient. A 'decision tree' is constructed first to show all the possible diagnoses. The tree is extended to show the possible interventional limbs into which the patient could be randomized, followed by all the possible outcomes of each treatment. The branches would end with the effect that each outcome would have on the overall well-being of the patient.

An estimate is then made of the proportions of patients with each diagnosis, the proportions opting for each treatment and the proportions of those experiencing various degrees of well-being. These proportions are then multiplied together to estimate the average degree of well-being experienced by patients sharing each treatment outcome. Each of these average degrees of benefit is regarded as the 'expected' degree of well-being that would be experienced by an individual patient with each outcome. This is regarded as a representation of what an experienced doctor would do when he or she estimates the effect on the patient of the different interventions available.[3, 4]

Medical science aims to provide diagnostic criteria, treatment indication criteria, and treatments that, when used together, will predict with a highest possible degree of certainty which treatment will work best for each patient (or would not help at all). This old aim is also the aim of 'stratified' or 'personalized' medicine. Such well-designed diagnostic systems would make it easier to choose the best option and to justify it using evidence in the form of data. This will not be possible without a clear understanding of the diagnostic process and criteria for confirming diagnoses that also indicate the best treatment for that patient as discussed in Chapter 13 (see ➔ Evidence-based diagnosis and decisions, p.616).

Diagnostic classifications, pathways, and tables

A diagnostic pathway or algorithm is a way of representing diagnostic reasoning processes or a diagnostic classification (see Fig. 1.1). The same reasoning processes can be displayed using a table of the kind shown in Table 1.1. This is also how information in this book is displayed. It is flexible and also allows findings to be shown that do not form part of the diagnostic criteria. The reader can scan down such a table to find the diagnoses that are compatible with the findings so far. The entry can then be copied into a table in the patient's records as a draft entry for that diagnostic possibility.

Table 1.1 Diagnostic table for the differential diagnoses of jaundice

Carotinaemia (not 'real' jaundice)	*Suggested by:* onset over months. Skin yellow with white sclerae, normal stools, and normal urine. Diet rich in yellow vegetables/fruits. *Confirmed by:* no bilirubin, no **urobilinogen** in the urine, and normal **serum bilirubin**. Normal **liver function tests (LFT)**. Response to diet change.
'Pre-hepatic' jaundice due to haemolysis	*Suggested by:* jaundice and anaemia (the combination seen as 'lemon' or pale yellow). Normal dark stools and normal-looking urine. *Confirmed by:* ↑(unconjugated and thus insoluble) **serum bilirubin**, but normal (conjugated and soluble) bilirubin and thus no ↑bilirubin in urine. ↑**urobilinogen in urine** and ↓**serum haptoglobin**. Normal LFT. ↑**reticulocyte count**.
'Hepatic' jaundice due to congenital enzyme defect	*Suggested by:* jaundice. Normal-looking stools and normal-looking urine. Jaundice worse during febrile illnesses. *Confirmed by:*↑**serum bilirubin** (unconjugated), but no (conjugated) bilirubin in urine. No **urobilinogen in urine** and **normal haptoglobin**. Normal **LFT**.
'Hepatocellular' jaundice ('hepatic' with some 'obstructive' jaundice)	*Suggested by:* onset of jaundice over days or weeks, pale stools but dark urine. *Confirmed by:* ↑serum (conjugated) **bilirubin** and thus ↑**urine bilirubin**. Normal **urine urobilinogen**. **LFT** all abnormal, especially ↑↑**ALT**.
'Obstructive' jaundice	*Suggested by:* onset of jaundice over days or weeks with pale stools and dark urine. Bilirubin (i.e. conjugated and thus soluble) in urine. *Confirmed by:* ↑ **serum conjugated bilirubin** and **urine bilirubin**, but no ↑**urobilinogen** in urine. Markedly (↑↑) **alkaline phosphatase**, but less abnormal (↑) **LFT** and ↑γ**GT**.

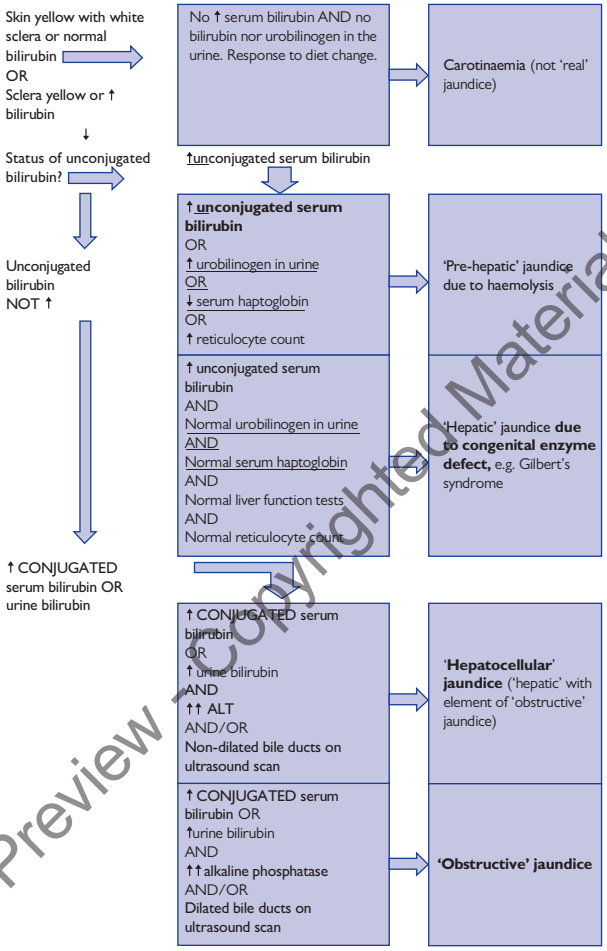

Fig. 1.1 A diagnostic pathway for jaundice.

Dynamic diagnoses

It is important to understand that clinical diagnosis is not a static classification system based on diagnostic criteria or their probable presence. It is a dynamic process. Diagnostic algorithms 'classify' patients by following a logical pathway based mainly on diagnostic criteria. Other systems predict the probable presence of diagnostic criteria. All these methods can be regarded as 'diagnosing' a snap-shot of what is happening at a particular time.

The diagnostician has to imagine the presence of a dynamic process that changes with time. There may be several processes taking place at the same time, some progressing over years (e.g. atheromatous changes), some over minutes to hours (e.g. a thrombosis in a coronary artery), some over minutes or seconds (e.g. ventricular tachycardia), and others instantaneously (e.g. a cardiac arrest).

A diagnostic process leading to treatment may have to happen in stages and for a number of diagnoses at the same time. It might be more appropriate to think of the process as one of 'feedback' control. In this way, the doctor would be acting as an external control mechanism support the patient's failing mechanisms. After the initial history and examination, the feedback information may come from electronic monitoring, nursing observations, ward rounds, hospital clinic, or primary care follow-up.

There are three types of mechanisms of interest to the diagnostician:

- Those that control the 'internal milieu' by keeping temperature, tissue perfusion, blood gases, and biochemistry constant.
- Those that control the body's structure by effecting repair in response to any damage.
- Those that control the 'external milieu' of day-to-day living.

These are all interdependent. If one mechanism fails, then it may unmask other weaknesses by causing other failures. It may not be enough to treat the main failure. It is often necessary also to treat the causes and consequences, as they may be unable to recover on their own. For example, a coronary thrombosis may be treated with stenting of the coronary artery, but any resulting rhythm abnormalities may need to be treated and also the causative risk factors (e.g. smoking) that could result in recurrence. So when we explain our diagnostic thought processes, it helps to think of each diagnosis as a subheading with its own evidence and decision.

The whole patient

A 'diagnosis' does not imply that only one solution needs to be discovered. The complete diagnosis (or diagnostic formulation) may have to include various causes, consequences, interactions, and other independent processes. As well as internal medical processes, it has to include external factors, such as circumstances at home and the effects on self-care, employment, and leisure.

There may be many diagnoses that have been confirmed previously and for which the patient is on established treatment. Therefore, the diagnostician must imagine what is happening to the 'whole patient'. This requires a broad medical education that allows a range of phenomena to be pictured, from molecular events to events in the home and outside world.

Explaining diagnoses to patients

The patient may already be imagining with some trepidation what might be happening. It is important to find out what the patient is imagining and to use this as a starting point for your own explanation. The patient's own views are usually sought and documented at the end of the history of the presenting complaint.

Patients and relatives usually ask questions spontaneously or request an appointment for time to be set aside to do this. Some may be too shy and need encouragement to do so, in which case this important aspect of care will be omitted. Others may be too ill to listen and may prefer relatives or carers to ask on their behalf. If questions are not asked spontaneously, it is best to ask patients tactfully if they or anyone else with their consent have any questions.

Although patients and relatives may understand explanations and other answers to questions at the time they are given to them, even the most intelligent may forget unfamiliar technical terms and their meaning within a short time, especially if they are ill. Therefore, it is important to provide a written reminder of such terms and how they are related. This can be done by giving the patient a printed summary similar to that in ➔ An evidence-based diagnosis and plan, p.13. This can also allow the patient to ask further questions if they wish.

Informed consent is also based on similar questions and discussion. The process is more effective if the patient is able to ask the questions (i.e. if the process is 'patient-centred'). Such a process may be facilitated if they refer to a summary such as that shown in ➔ An evidence-based diagnosis and plan, p.13.

Ideally, patients should know the presenting complaint for their latest problems, the primary diagnosis or differential diagnoses, and what actions are being taken in terms of tests and treatments. They should also be aware of their past medical history: the various diagnoses, how they presented and were confirmed, their treatments, follow-up arrangements, and markers of progress. Again, the relevant technical terms and how they are linked can be summarized for them as shown in ➔ An evidence-based diagnosis and plan, p.13.

Informed consent

In order for a patient to consent to treatment, he or she must understand what has been said and be able to retain that explanation. A basic understanding means the patient must know what actions have been agreed and the possible diagnoses in each case. In order to understand each diagnosis, it is essential to know which symptoms it explains and how these symptoms or some other markers are progressing. Few patients are able to retain all of this, especially if there are many technical terms that are unfamiliar to them. Therefore, it would be a sensible policy to provide the patient with a typed explanation setting out these basic relationships as shown in ➔ An evidence-based diagnosis and plan, p.13. This would then become the next 'past medical history' when the patient is asked to provide it by another doctor or nurse. It would thus allow patients to ask a doctor or nurse to remind them of the meanings of the various terms.

Minimizing diagnostic errors

The diagnostic and decision-making process usually takes place in busy clinics, wards, operating theatres, and emergency rooms. Therefore, most diagnoses have to take place by some rapid conscious or subconscious pattern recognition, and there is usually little time for reflection. Mistakes are kept to a minimum by good training, especially listening carefully and writing out what has been observed, thought, and done.

Another important principle to bear in mind is that even the most expert and well-founded diagnoses and decisions can only be successful in a proportion of cases. Therefore, there must be a strategy to monitor their outcome and to change diagnoses and decisions, if possible.

Diagnostic errors can be classified in terms of cognitive psychology[3] into:

- Faulty triggering
- Faulty context information
- Faulty verification
- No fault errors
- Faulty information gathering and processing.

Faulty triggering

This is a failure to consider appropriate diagnostic possibilities, often attributed to a weakness of medical education, which focuses on disease processes instead of the diagnostic processes. This type of error can be kept to a minimum by using the suggestions in the sections from ➔ 'Transparent' reasoning, p.5 to ➔ An evidence-based diagnosis and plan, p.13, and by referring to the differential diagnoses in the other sections. Finally, this error can be reduced by not only writing down the differential diagnoses, but also by writing down the findings from which were chosen the leads that 'triggered' them as shown in ➔ An evidence-based diagnosis and plan, p.13. This can be given to the patient to be shown to other doctors who might also spot any omissions.

Faulty context information

This is focusing on one diagnosis and failing to consider others that may also be present. It involves jumping to conclusions. This can be avoided by using the sieves in ➔ Medical and surgical sieves, p.14, referring to the appropriate section in this book, and writing out an overall plan as shown in ➔ An evidence-based diagnosis and plan, p.13, so that other doctors might spot any errors. Again, this can be given to the patient (to show to other doctors who might spot any errors).

Faulty verification

This is failure to ensure that the patient's presenting symptom and other markers of poor health have been controlled or stabilized as well as possible. This is discussed in ➔ Confirming and finalizing a diagnosis, p.8. It also helps to set out each diagnosis with its evidence as shown in ➔ An evidence-based diagnosis and plan, p.13, which includes the markers being followed and their latest results. Again, this summary can be given to the patient to be shown to other doctors who might spot such omissions.

No fault errors

Even the most expert and well-founded diagnoses and decisions can only be successful in a proportion of cases. This is why diagnoses and decisions are qualified with probabilities. Therefore, there must be a strategy to monitor the outcome of all diagnoses and decisions and to change them, if possible. If a summary of the kind shown in ➔ An evidence-based diagnosis and plan, p.13 is given to the patient to be shown to other doctors, they will be able to understand the basis of previous decisions and take appropriate action.

Faulty information gathering and processing

This is poor use of leads and differentiators in appropriate settings. This book focuses on this process. It is important to know the differential diagnoses of leads and the frequency with which they occur in different clinical settings. It is also important to know the frequency with which findings occur in pairs of diagnoses. At present, this is gained from personal experience. Little research is done into diagnostic leads, differential likelihood ratios, optimizing treatment indication, and diagnostic criteria because the main focus of research is currently on sensitivity, specificity, and overall likelihood ratios. The way in which the situation can be improved is outlined in Chapter 13 (see ➔ Evidence-based diagnosis and decisions, p.616).

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