An outline of CLINICAL DIAGNOSIS

Brian J Prout
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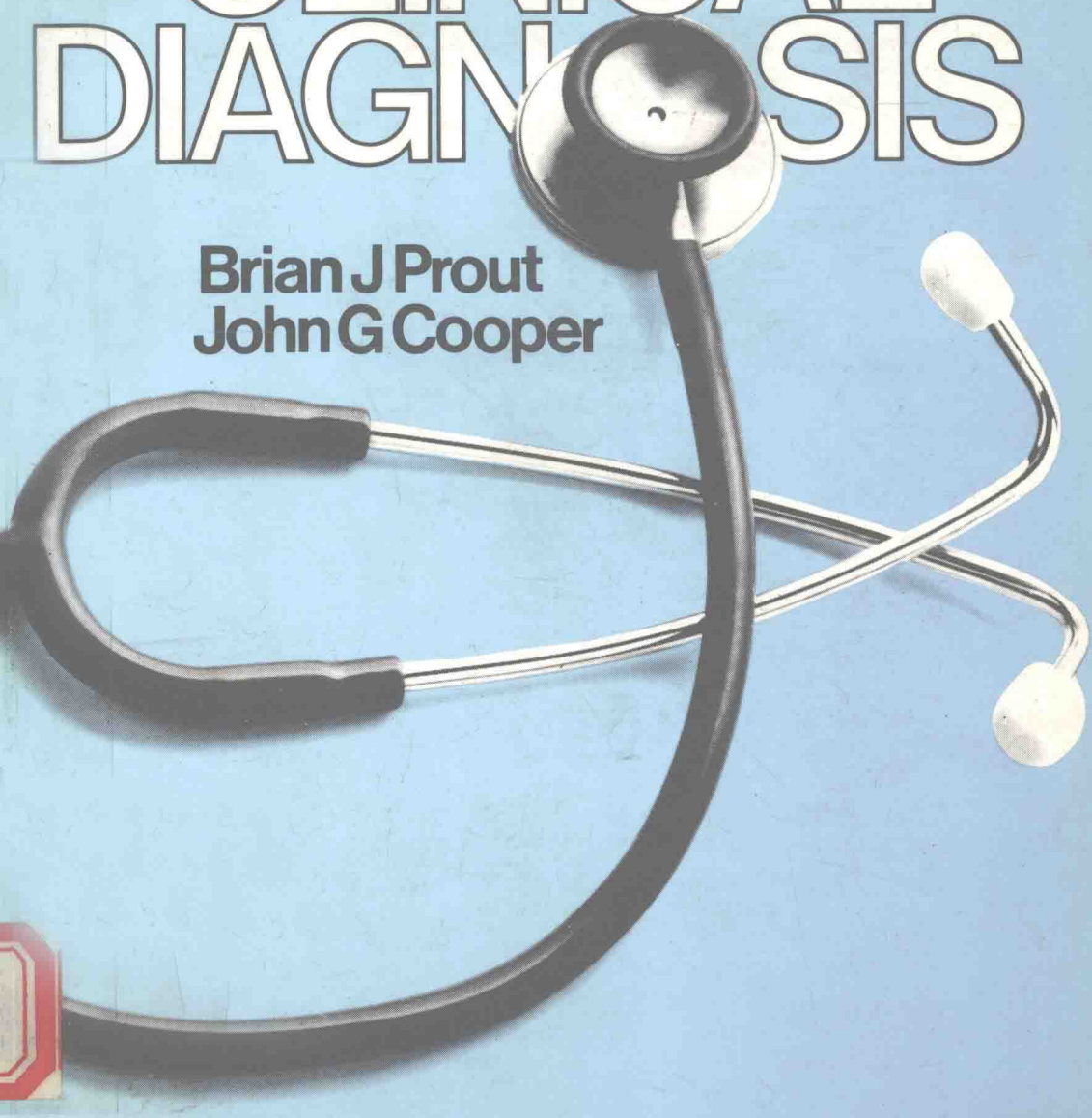

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To my wife Jane

and daughters
Nicola and Deborah

BJP

Preface

This book gives an outline of the procedure to follow in the diagnosis of the more common clinical problems as they present in the patient. It is hoped that a wide range of students and physicians will find the book a useful practical guide, and revision text for examination.

Some investigations, particularly in the later stages of making a diagnosis, can only be carried out in hospital, but we hope that physicians starting out in general practice and family practice will also find that they can follow the diagnostic steps taken with a particular problem. In many cases they will be able to make a diagnosis at an early stage.

At the end of each chapter there is a flow diagram summarizing the steps in investigation and making a diagnosis. Quite clearly, a routine blood count or urine analysis will always precede isotopic or angiographic studies. At times, however, the order in which one sets about investigating a problem is not always so clear cut, and juniors in particular need to be reminded that sensible order in investigation is vital.

In this book, we have not tried to be absolutely comprehensive, but to select some of the more common problems that physicians will face in modern clinical practice. The choice of chapters has meant considerable thought in order to avoid repetition of subject matter or procedure. For example, 'Change of bowel habit' has been included but 'Rectal bleeding' has not, because the diagnostic procedures are similar, except for the need to exclude bleeding disorders in the latter. Bleeding will be found as a clinical problem in its own right.

Where there are tables the items are given so as to indicate the more common at the top of the list. Wherever possible the more common causes for a symptom or condition are printed in bolder type. Because of regional variations this distinction cannot also be clear cut – for example, leprosy is a common cause of neuropathy in an endemic area but rare in a Western European community.

We hope that the clinical points in the margins will provide valuable hints and guidance to our readers and keep alive the practical nature of patient care.

The Authors

Dr Brian J Prout spent some years teaching at the London teaching hospitals and in Oxford, before taking up the post of Consultant Physician at the Royal Cornwall Hospital, Truro. He continues to hold regular tutorials and seminars for students, hospital junior staff and general practitioners. The idea for this symptom-orientated book arose from these sessions.

Dr John G Cooper had teaching experience in a London teaching hospital and in Manchester before taking the post of Registrar in General Medicine at the Royal Cornwall Hospital. He has recently moved to a post at the Hamer Hospital in Norway.

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Contents

Pyrexia of unknown origin

1

Pyrexia of unknown origin (PUO) is an unexplained fever recorded on several occasions over a three-week period or longer. In many reported series of PUO additional criteria have been a temperature greater than 38·4 °C for which an adequate cause has not been found and which remains undiagnosed after a week of in-patient investigations. This definition excludes all fevers of short duration and those in which the cause is obvious.

In most cases of PUO the underlying cause can eventually be found, but the hospital stay will be unnecessarily long if the plan of investigation is not reviewed frequently as new information becomes available. In most published series the diagnostic categories of PUO are similar.

- Infection 40%
- Neoplastic disease 20%
- Connective tissue disorder 20%
- Rare disease or undiagnosed 20%

Initial assessment

After a general medical history the following special enquiries are made:

- Foreign travel — *see Table* 1.1
- Occupation and animal contacts — *see Table* 1.2
- Alcohol intake
- Recent exposure to infection
- Previous illnesses
- Previous surgery or accidents
- Familial disorders
- Drug usage

Table 1.1. Incubation periods of some pyrexial tropical diseases which may be imported to Britain

Less than 10 days
Yellow fever
Typhus (tick-borne)
Paratyphoid
Dengue
Up to 21 days
Typhus (mite-borne)
Smallpox
Malaria
Typhoid
Brucellosis
Lassa fever
African trypanosomiasis
More than 21 days
Hepatic amoebiasis
Viral hepatitis
Kala-azar
Filariasis
Rabies

No complaint even if apparently trivial in nature, whether volunteered or elicited by questioning, should be disregarded, e.g. mild abdominal discomfort may be the first symptom of lymphoma or abdominal abscess.

During the subsequent general examination the following indicate the physical signs which should not be missed:

- Dental or oropharyngeal sepsis
- Eye signs (conjunctival petechiae, choroidal deposits)
- Temporal artery or scalp tenderness
- Skin lesions (rashes; small infarctions; ulcers; petechiae)
- Epitrochlear lymphadenopathy
- Grossly enlarged abdominal organs (especially spleen)
- Hepatic bruit, or friction rub
- Unobtrusive cardiac murmurs
- Gynaecological lesions

The patient's weight should be recorded at the outset and weekly and documented clearly with the 4-hourly temperature and pulse chart.

Routine rectal examination should be followed by sigmoidoscopy with biopsy if bowel symptoms are present. In other situations rectal biopsy is valuable

Table 1.2. Some febrile illnesses acquired from animals

Leptospirosis	Rats, dogs, pigs, foxes, mice, voles
Q fever	Cattle, sheep, goats, dogs, birds
Salmonellosis	Dogs, cats, pigeons, tortoises, terrapins
Cat-scratch fever	Cats
Psittacosis and ornithosis	Parrots, budgerigars, pigeons, canaries, domestic fowl
Toxoplasmosis	Cats, dogs, farm animals
Hydatid disease	Sheep, horses, dogs, cats
Canicola fever	Dogs
Toxocariasis	Dogs, cats
Meningitis and septicaemia (due to *Strep. suis*)	Pigs
Trichiniasis	Pigs, rodents, wild animals
Tularaemia	Rodents, rabbits, hares
Anthrax	Sheep, goats, cattle, pigs, horses, wild animals (hide, hair, bone products, etc.)

in suspected amyloid disease and vital in suspected schistosomiasis.

Following the initial assessment appropriate laboratory tests may be immediately indicated, e.g. the examination of thick and thin blood films in someone who has been to malarial parts of the world. If no diagnostic lead is discovered, the investigation must proceed as systematically as possible and all non-essential drugs should be stopped at this stage.

The initial basic screening tests to be performed are relatively non-specific but in most cases will suggest the area for more definitive investigation. They are followed by more specific or second level tests.

Basic screening tests

- Full blood count with differential cell count
- ESR or serum viscosity
- Examination of thick blood film for parasites (visitors from malarial areas or tropics)
- Liver function tests
- Urine analysis, microscopy and culture
- Faeces culture
- Blood cultures

- Vaginal and cervical cultures in women
- Throat swab culture
- Acute phase serological studies
- Chest X-ray
- Plain abdominal X-ray

The initial tests may give clues to the diagnosis and are best summarized as follows:

Clues to diagnosis on initial tests

Haematology

- Neutrophil leucocytosis
  Possible bacterial infection
- Leucopenia
  Brucellosis
  Lymphoma
  Systemic lupus erythematosus (SLE)
- Monocytosis
  Subacute bacterial endocarditis (SBE)
  Tuberculosis
  Brucellosis
  Inflammatory bowel disease
  Solid tumours
  Hodgkin's disease
- Abnormal mononuclear cells with lymphocytosis
  Glandular fever
  Toxoplasmosis
  Cytomegalovirus infection
- Eosinophilia
  Parasitic infection
  Reticulosis
- ESR > 50 mm/1 hr
  1. Giant-cell arteritis
  2. Still's disease
  3. Rheumatic fever
  4. Lymphoma
  5. SLE
  6. SBE

◀ The ESR may be raised in SBE only in the absence of heart failure.

◀ A normal ESR makes any of the conditions (1–6) unlikely but does not exclude them.

Biochemistry

- Liver function tests
  May indicate liver disease
- Alkaline phosphatase raised
  Liver disease
  Bone disease
  Hodgkin's disease
  Still's disease
  Hypernephroma

▼ **Clinical points**

- Immunoglobulin raised
  IgG — SLE and chronic hepatitis
  IgM — Viral hepatitis after acute phase
  IgA — Crohn's disease

Bacteriology and Serology

- Urine cultures and microscopy
  May reveal bacteria or haematuria suggesting causes of fever such as hypernephroma or SBE.
- Blood culture
  Anaerobic and aerobic cultures three times on the first two days. In addition, after open heart surgery, arterial blood cultures are indicated. This may reveal the organism infecting the blood stream.

◀ Beware of contaminated blood cultures giving false positives.

- Serology
  Specific diagnostic tests are available for a large range of infections; some examples are:
  Glandular fever
  Toxoplasmosis
  Q fever
  Psittacosis
  Brucellosis
  Typhoid and paratyphoid
  Cytomegalovirus and other viruses
  Leptospirosis

◀ The Widal test is not specific for typhoid infection and the best confirmation of infection with ***S. typhi*** is to culture it from the stool.

Other serological tests for other exotic infections may later be indicated.

Second estimations of antibody titres should follow in 10–21 days.

◀ Negative or rising antibody titres are most helpful.

Antibody tests for the presence of immune disorders:

- Antinuclear antibodies
- Rheumatoid factor
- Complement levels
- Antistreptolysin titre

Radiology

1. Chest X-ray
   The chest X-ray should be checked in a systematic manner:
   a. Lung fields
   b. Hilar shadows
   c. Bone
   d. Cardiac configuration
   Special points to note in viewing the chest X-ray are:
   - Apical fibrosis or calcification raises the possibility of tuberculosis elsewhere

▼ **Clinical points**

- A normal chest X-ray does not exclude tuberculous infection
- Look for calcification of cardiac valves or prosthetic valve
- A diaphragm abnormality may indicate thoracic or abdominal disease. If so, check diaphragm movement by screening

◀Percuss the chest posteriorly to check if the diaphragm is moving. When in doubt check with radiological screening.

2. Abdominal X-ray
   Study the abdominal X-ray for:
   a. Abnormal calcification
   b. Enlargement of organs
   c. Loss of psoas shadow
   d. Abnormal bone
   e. Abnormal shadows
3. Skull X-ray, paranasal sinuses X-ray and panoral X-ray views of teeth. There may be signs of infection or malignancy in the cranial bones or within the sinuses. Apical dental abscess is particularly relevant in suspected SBE

At this point it is helpful to carry out the first of a series of tuberculin skin tests starting with the most dilute in case a strong reaction occurs. In tuberculosis the tuberculin skin test may be negative and repeated early morning specimens or urine, sputum and gastric washings should be examined for mycobacteria.

In suspected sarcoidosis the Kveim test is useful and should be performed early because of the waiting time before biopsy. The biopsy should be interpreted by an expert.

◀A negative Kveim test does not exclude sarcoidosis.

One may now be aware of the site of the problem and it remains to differentiate it further by the second level of tests.

Second-level tests

If a liver problem is suspected:

Check

Liver ultrasound.

Using this technique it is possible to demonstrate abnormalities in the liver and biliary tree as well as the pancreas. If used in conjunction with gallium-67 scanning further details can be visualized.

Radionuclide liver scan.

Using technetium-99 in labelled colloid the whole liver can be studied but lesions <2 cm in diameter

▼ **Clinical points**

may not be visualized. Gallium-67 is, however, taken up by neoplastic and inflammatory lesions.

Needle biopsy.

Histological examination is valuable in diagnosing the type of liver disease and also gives information about systemic diseases affecting the liver.

◀ Primary or secondary hepatic tumours can cause PUO.

◀ Remember to culture a portion of the liver biopsy including culture and microscopy for tubercle bacilli and fungi.

If a renal problem is suspected:

Intravenous urography.

This will outline the kidneys, provided severe renal failure is not present.

Renal ultrasound.

The right kidney may be visualized in the scan of the liver.

Renal arteriography.

This is occasionally helpful to delineate abnormal lesions seen in the other investigations.

◀ Hypernephroma, TB, intrarenal or perinephric abscess can cause PUO.

◀ Beware of carrying out an intravenous urogram if the patient might have myeloma.

If a pulmonary problem is suspected:

Check

Ventilation and perfusion radionuclide lung scan

Pulmonary angiography

Both these techniques are valuable in demonstrating pulmonary infarction

◀ Multiple pulmonary emboli can cause PUO.

If a gastro-intestinal problem is suspected:

Check

Barium enema

Barium meal

Small bowel series

Cholecystogram

◀ Gallstones may be an incidental finding.

◀ Inflammatory bowel disease can cause PUO.

If a reticulosis is suspected:

Check

Biopsy of enlarged lymph glands or scalene node; liver; marrow.

As well as histological examination remember to culture biopsy material for bacteria (including Brucella); mycobacteria; fungi.

Lymphangiogram of suspected area.

This may in some centres be replaced by CT scanning which is probably more accurate.

◀ Always culture biopsy material in PUO.

◀ The culture yield of bone marrow is higher than from peripheral blood in partially treated bacterial endocarditis.

▼ **Clinical points**

If a cardiac lesion is suspected:

The application of echocardiography may reveal heart valve vegetations; atrial myxoma.

If a pelvic intra- or retroperitoneal mass is suspected:

The use of CT scanning, ultrasound, or gallium scanning of the suspected area may visualize the lesion.

Some cases of PUO remain obscure after considerable investigation. Examples of cases which have been difficult to diagnose include:

- Endocrine abnormalities (hyperthyroidism, phaeochromocytoma and Addison's disease)
- Granulomatous hepatitis (which may present with normal liver function tests and be overlooked as a possibility)
- Still's disease
- Whipple's disease
- Adenocarcinoma of the colon
- Familial Mediterranean fever

Factitious fever may be difficult to diagnose. Patients who manipulate either their body temperature or the thermometer are often, but not exclusively, young females with a paramedical occupation.

Clues to the diagnosis of factitious fever are:

- Inappropriately low heart rate at a febrile temperature
- Lack of weight loss or other evidence of chronic illness
- Abrupt changes in temperature unaccompanied by chills or sweating

The diagnosis can be confirmed by observed temperature measurement and simultaneous measurement of oral and rectal or urinary temperature. There is usually an underlying psychological disorder.

If the PUO remains unexplained after thorough investigation, there are three choices available:

1. *Laparotomy* which carries a high morbidity in patients with PUO
2. *Therapeutic trial*. This usually takes one of three forms depending upon what the most likely diagnosis appears to be:

◀ There may be post-operative complications in 15–20 per cent of patients with PUOs subjected to laparotomy.

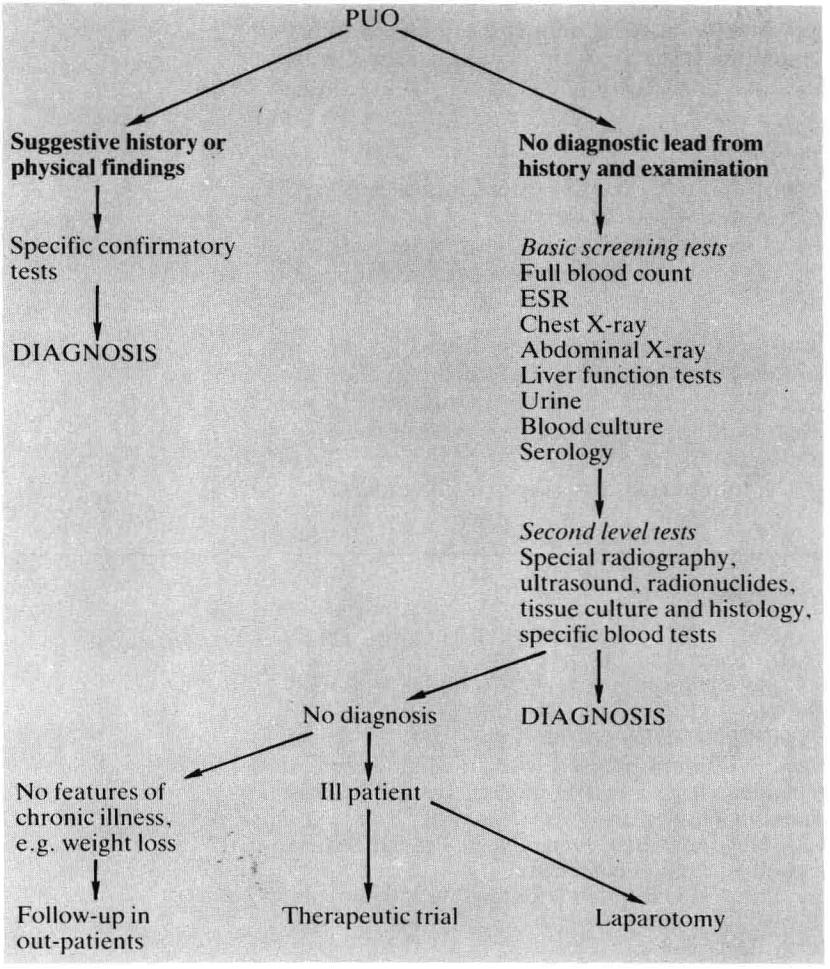

Fig. 1.1 Stages in the diagnosis of PUO.

a. Administration of steroids (prednisolone 40–60 mg daily on a reducing regimen).
b. Salicylates at high dosage.
c. Antibiotics (penicillin and aminoglycoside or antituberculous therapy if TB is suspected).

3. *Discharge from hospital*

Up to 10 per cent PUOs have remained undiagnosed after thorough investigation in large centres. In most cases prolonged follow-up shows that the fever resolves and no diagnosis is ever made. Weight loss is a useful indication of underlying