

# best tests

**Complete Blood Count**

**June 2008**

**Making Sense of Blood Films**

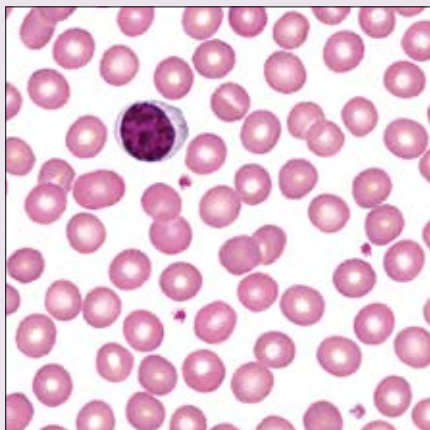
**Summary: Complete Blood Count in Primary care**

**Drug Induced Agranulocytosis**

## Making sense of blood films

The following blood films have characteristic features. For each case, the cell counts are provided, along with the blood film comment. For each set of results, determine the most likely diagnosis.

Results are on the back page.



**Case 1:** 18 year old woman, blood test prior to year in Germany as an AFS exchange student. Clinical examination: NAD.

**Cell Counts:**

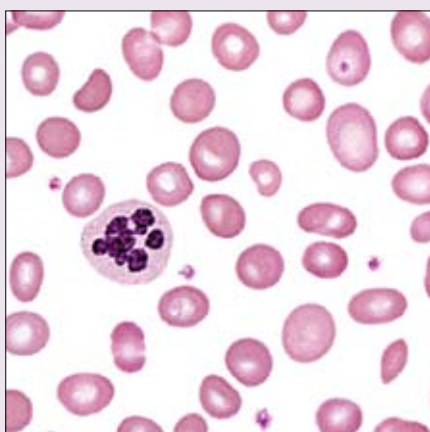
Hb:	132 g/L	N	PCV:	0.36	N
MCV:	85 fl	N	MCH:	28 pg	N
WBC	$5.9 \times 10^9/L$	N	Plt:	$286 \times 10^9/L$	N

**Blood film:**

RBC morphology: normocytic, normochromic.

WBC morphology: within normal limits.

Platelet morphology: within normal limits.



**Case 2:** 67 year old man complaining of tiredness and lightheadness. Clinical examination: appears pale otherwise NAD, Meds: phenytoin – last 15 years, Social hx: widowed, poor nutrition

**Cell Counts:**

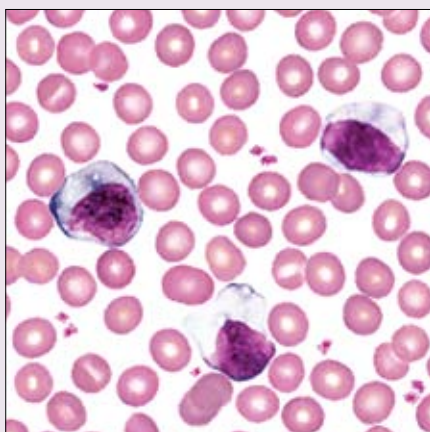
Hb:	79 g/L	↓	PCV:	0.23	↓
MCV:	114 fl	↑	MCH:	37 pg	↑
WBC	$6.2 \times 10^9/L$	N	Plt	$219 \times 10^9/L$	N

**Blood film:**

RBC morphology: normochromic, macrocytosis +++, anisocytosis +++, numerous oval macrocytes, occ teardrops and fragments.

WBC morphology: many neutrophils show nuclear hypersegmentation.

Platelet morphology: within normal limits.



**Case 3:** 19 year old male, fatigue, sore throat and fever.

Physical exam: enlarged tonsils, swollen cervical lymph nodes.

**Cell Counts:**

Hb:	154 g/L	N	PCV:	0.46	N
MCV:	88 fl	N	MCH:	29 pg	N
WBC	$12.9 \times 10^9/L$	↑	Plt	$333 \times 10^9/L$	N

WBC differential: N 24%, L 73%, M 0%, E 3%, B 0%

**Blood film:**

RBC morphology: normochromic, normocytic.

WBC morphology: most of the lymphocytes are large variant cells.

Platelet morphology: within normal limits.

## Summary: Complete Blood Count in Primary Care

Cell	High	Low
<b>Neutrophils</b>	<p>Most common causes:</p> <ul style="list-style-type: none"> <li>▪ Infection/inflammation</li> <li>▪ Necrosis</li> <li>▪ Any stressor/heavy exercise</li> <li>▪ Drugs</li> <li>▪ Pregnancy</li> <li>▪ CML</li> <li>▪ Smoking</li> <li>▪ Malignancy</li> </ul> <p>Red flags:</p> <ul style="list-style-type: none"> <li>▪ Person particularly unwell</li> <li>▪ Severity of neutrophilia</li> <li>▪ Rate of change of neutrophilia</li> <li>▪ Presence of left shift</li> </ul>	<p>Significant levels:</p> <ul style="list-style-type: none"> <li>▪ <math>&lt; 1.0 \times 10^9/L</math> (high risk infection)</li> </ul> <p>Most common causes:</p> <ul style="list-style-type: none"> <li>▪ Viral (overt or occult)</li> <li>▪ Autoimmune/idiopathic</li> <li>▪ Medications</li> </ul> <p>Red flags:</p> <ul style="list-style-type: none"> <li>▪ Person particularly unwell</li> <li>▪ Severity of neutropenia</li> <li>▪ Rate of change of neutropenia</li> <li>▪ Lymphadenopathy, hepatosplenomegaly</li> </ul>
<b>Lymphocytes</b>	<p>Causes:</p> <ul style="list-style-type: none"> <li>▪ Acute infection (viral, bacterial)</li> <li>▪ Smoking</li> <li>▪ Hyposplenism</li> <li>▪ Acute stress response</li> <li>▪ Autoimmune thyroiditis</li> <li>▪ CLL</li> </ul>	Not usually clinically significant
<b>Eosinophils</b>	<p>Most common causes:</p> <ul style="list-style-type: none"> <li>▪ Allergy/atopy, asthma/hayfever</li> <li>▪ Parasites (less common in developed countries)</li> </ul> <p>Rarer causes:</p> <ul style="list-style-type: none"> <li>▪ Hodgkins</li> <li>▪ Myeloproliferative disorders</li> <li>▪ Churg-Strauss syndrome</li> </ul>	No real cause for concern
<b>Monocytes</b>	<ul style="list-style-type: none"> <li>▪ Usually not significant</li> <li>▪ Watch levels <math>&gt; 1.5 \times 10^9/L</math> more closely</li> </ul>	Not clinically significant
<b>Basophils</b>	<p>Associated with:</p> <ul style="list-style-type: none"> <li>▪ Myeloproliferative disorders</li> <li>▪ Other rare causes</li> </ul>	Difficult to demonstrate
<b>Platelets</b>	<p>Significant levels:</p> <ul style="list-style-type: none"> <li>▪ <math>&gt; 500 \times 10^9/L</math></li> </ul> <p>Most likely causes:</p> <ul style="list-style-type: none"> <li>▪ Reactive conditions e.g. infection, inflammation</li> <li>▪ Pregnancy</li> <li>▪ Iron deficiency</li> <li>▪ Post splenectomy</li> <li>▪ Essential thrombocythaemia</li> </ul>	<p>Significant levels:</p> <ul style="list-style-type: none"> <li>▪ <math>&lt; 100 \times 10^9/L</math></li> </ul> <p>Most common causes:</p> <ul style="list-style-type: none"> <li>▪ Viral infection</li> <li>▪ Idiopathic thrombocytopenic purpura</li> <li>▪ Liver disease</li> <li>▪ Drugs</li> <li>▪ Hypersplenism</li> <li>▪ Autoimmune disease</li> <li>▪ Pregnancy</li> </ul> <p>Red flags:</p> <ul style="list-style-type: none"> <li>▪ Bruising</li> <li>▪ Petechiae</li> <li>▪ Signs of bleeding</li> </ul>

## Drug induced agranulocytosis

The consequences of drug-induced agranulocytosis can be life threatening, but it is reassuring that it is a relatively rare occurrence. A recent systematic review<sup>1</sup> has revealed 125 drugs that either definitely or probably cause acute agranulocytosis. Although different sources mention different drugs, those most often associated with a higher risk of agranulocytosis include: carbimazole, clozapine, sulphasalazine, gold salts, penicillamine and clopidogrel.<sup>2</sup> In most cases, drug induced acute agranulocytosis occurs within the first three months of starting the drug.

The onset of agranulocytosis is abrupt and patients receiving medications associated with high risk should be warned to **seek medical advice urgently if they develop fever, sore throat or other infection**. Written instruction may be useful for some patients.

Requirements for monitoring vary depending on the medication, and can be obtained from sources such as BNF or MIMs.

### References:

1. Andersohn F, Konzen C, Garbe E. Systematic review: Agranulocytosis Induced by Nonchemotherapy Drugs. *Ann Intern Med* 2007;146:657-665.
2. Andrès E, Zimmer J, Affenberger S, et al. Idiosyncratic drug-induced agranulocytosis: Update of an old disorder. *Eur J Intern Med* 2006;17(8):529-35.

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## Blood film discussions

### Case 1: Normal blood film

Note red cells of fairly even size, shape, colour and area of central pallor.

### Case 2: Megaloblastic anaemia caused by folate deficiency

This picture is characteristic of a megaloblastic anaemia, which are most frequently caused by either vitamin B12 or folate deficiency. The CBC may reveal a number of distinctive changes, for example, the haemoglobin will be low, and MCV and MCH both elevated, the blood film may reveal oval macrocytes (instead of round), and hypersegmented neutrophils (often present in nutritional megaloblastic anaemias). Tests for vitamin B12 and folate should be requested for confirmation.

For this case, phenytoin is known to interfere with folate utilisation, and in combination with the recent poor diet, folate deficiency has developed. Folate deficiency can develop faster than B12 deficiency, with most people having stores for 6 months compared to 3–6 years for vitamin B12. Adequate folate intake can restore folate levels within a few days.

### Case 3: Infectious mononucleosis

The presence of a lymphocytosis with variant lymphocytes in a patient aged 10 to 30 years with sore throat, fever and fatigue is highly suggestive of infectious mononucleosis, and some believe this presentation is diagnostic. However, if the diagnosis is still uncertain, additional tests are available. Heterophilic antibodies (Paul Bunnell, Monospot) will test positive in 90% of people by the third week of illness, persisting for 3–6 months. Where clinical suspicion is high and heterophilic antibodies continue to test negative, EBV antibodies may be requested (although these are considerably more expensive). The presence of IgM antibodies indicate current or recent infection, while IgG antibodies persist for life.

