QUESTION 65
A 36-year-old man presents in a post-ictal state after an observed generalised seizure.
Full blood investigation shows:

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>haemoglobin</td>
<td>90 g/L [128-175]</td>
<td></td>
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<tr>
<td>mean corpuscular volume (MCV)</td>
<td>106 fL [80-97]</td>
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<tr>
<td>white cell count</td>
<td>12.6 x 10^9 /L [3.9-12.7]</td>
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<tr>
<td>differential:</td>
<td></td>
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<tr>
<td>neutrophils</td>
<td>10.4 x 10^9 /L [1.9-8.0]</td>
<td></td>
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<tr>
<td>lymphocytes</td>
<td>0.8 x 10^9 /L [0.9-3.3]</td>
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<tr>
<td>monocytes</td>
<td>1.1 x 10^9 /L [0.3-1.1]</td>
<td></td>
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<tr>
<td>eosinophils</td>
<td>0.2 x 10^9 /L [0-0.5]</td>
<td></td>
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<tr>
<td>basophils</td>
<td>0.1 x 10^9 /L [0-0.1]</td>
<td></td>
</tr>
<tr>
<td>platelet count</td>
<td>135 x 10^9 /L [150-396]</td>
<td></td>
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</tbody>
</table>

The blood film is shown below.

The most likely cause of the peripheral blood macrocytosis is:
A. β-thalassaemia trait.
B. myelodysplasia.
C. alcoholic liver disease.
D. hereditary spherocytosis.
E. myelofibrosis.

Anaemia – macrocytic
Slight thrombocytopenia
Target cells +++

Alcoholic Liver Disease

- target cells

Liver disease, particularly if caused by alcohol, is a common cause of macrocytosis, which is often accompanied by target cell formation. The mechanism is not known but increased lipid deposition on red cell membranes, similar to that seen in hyperlipidemia may be involved.
Peripheral smear shows multiple target cells which have an area of central density surrounded by a halo of pallor (arrows). These cells are characteristic of liver disease and certain hemoglobinopathies (most notably hemoglobin C disease).

Beta thalassemia trait
- Anaemia,
- Microcytosis - decreased MCV

Features
- Profound microcytic anemia (3-4 g)
- Bizarre red cell morphology is a hallmark of this syndrome
- Extreme hypochromia and poikilocytosis, a predominance of microcytes, tear drop and target cells
- The white blood cell (WBC) count is often strikingly high, and the reticulocyte count surprisingly low, reflects the severe degree of ineffective erythropoiesis underlying the disorder, resulting in many fewer than the expected number of reticulocytes being released from the bone marrow.
- The platelet count is usually normal. However, hypersplenism can lower both white cell and platelet counts.
- Because of the high rate of erythroid cell turnover, the serum iron level is usually elevated; the transferrin saturation, expressed as the ratio of serum iron to total iron binding capacity (or transferrin), is very high. The serum is often icteric, and increased concentrations of indirect (unconjugated) bilirubin and lactate dehydrogenase, and low levels of haptoglobin, findings typical of hemolytic disease, are usually present.
Peripheral smear from a patient with beta thalassemia intermedia post-splenectomy. This field shows target cells, hypochromic cells, microcytic cells, red cell fragments, red cells with bizarre shapes, and a single nucleated red cell (arrow).

Myelodysplasia
- Dysplastic changes
- Neutrophilia

Virtually all patients with the myelodysplastic syndrome will have macrocytic anemia at presentation, along with varying degrees of neutropenia, monocytosis, circulating blast forms, reticulocytopenia, and thrombocytopenia.

Myelodysplastic syndromes, in their early stages, may be a common cause of apparently idiopathic macrocytic anemia, particularly in elderly patients.

Hereditary spherocytosis
- Spherocytes on film and bm (round no central pallor)

Routine blood counts in HS reveal anemia and reticulocytosis to varying degrees, depending upon the severity of the mutation. The usual reticulocyte count is from 5 to 20 percent. The mean corpuscular volume (MCV) is normal or slightly low and is of little diagnostic value. However, considering the degree of reticulocytosis, the MCV is actually low.

The most helpful red cell index is the mean cell hemoglobin concentration (MCHC) which is routinely elevated, reflecting membrane loss and red cell dehydration.
Peripheral blood smear shows multiple spherocytes which are small, dark, dense hyperchomic red cells without central pallor (arrows). These findings are compatible with hereditary spherocytosis or autoimmune hemolytic anemia.

Myelofibrosis
- Bone marrow fibrosis
- Pancytopenia
- Tear drop cells
- Blasts

- Anemia with hemoglobin less than 10 gm causes include:
  - Reduction in medullary erythropoietic sites Ineffective erythropoiesis associated with extramedullary sites of red blood cell (RBC) production
  - Splenic sequestration and destruction of circulating RBCs Bleeding due to thrombocytopenia or other complications such as varices resulting from portal vein thrombosis
  - Autoimmune hemolysis
  - Dilutional “anemia” may be present in patients with large spleens and expanded plasma volumes, but normal red blood cell mass.

- The platelet and white blood cell (WBC) counts are variable
- Thrombocytopenia becomes more common with disease progression.
Leukoerythroblastic peripheral blood smear showing the presence of nucleated red cells and immature white cells. This pattern occurs with marrow replacement, usually due to fibrosis that may be idiopathic (eg, myelofibrosis with agnogenic myeloid metaplasia) or reactive to conditions such as metastatic cancer.

This peripheral smear from a patient with bone marrow fibrosis shows numerous teardrop-shaped red cells (arrows). Note that the teardrops are pointed in several different directions, ruling out an artifact due to preparation of the smear.
Bone marrow biopsy in myelofibrosis shows replacement of the marrow with fibrous tissue.