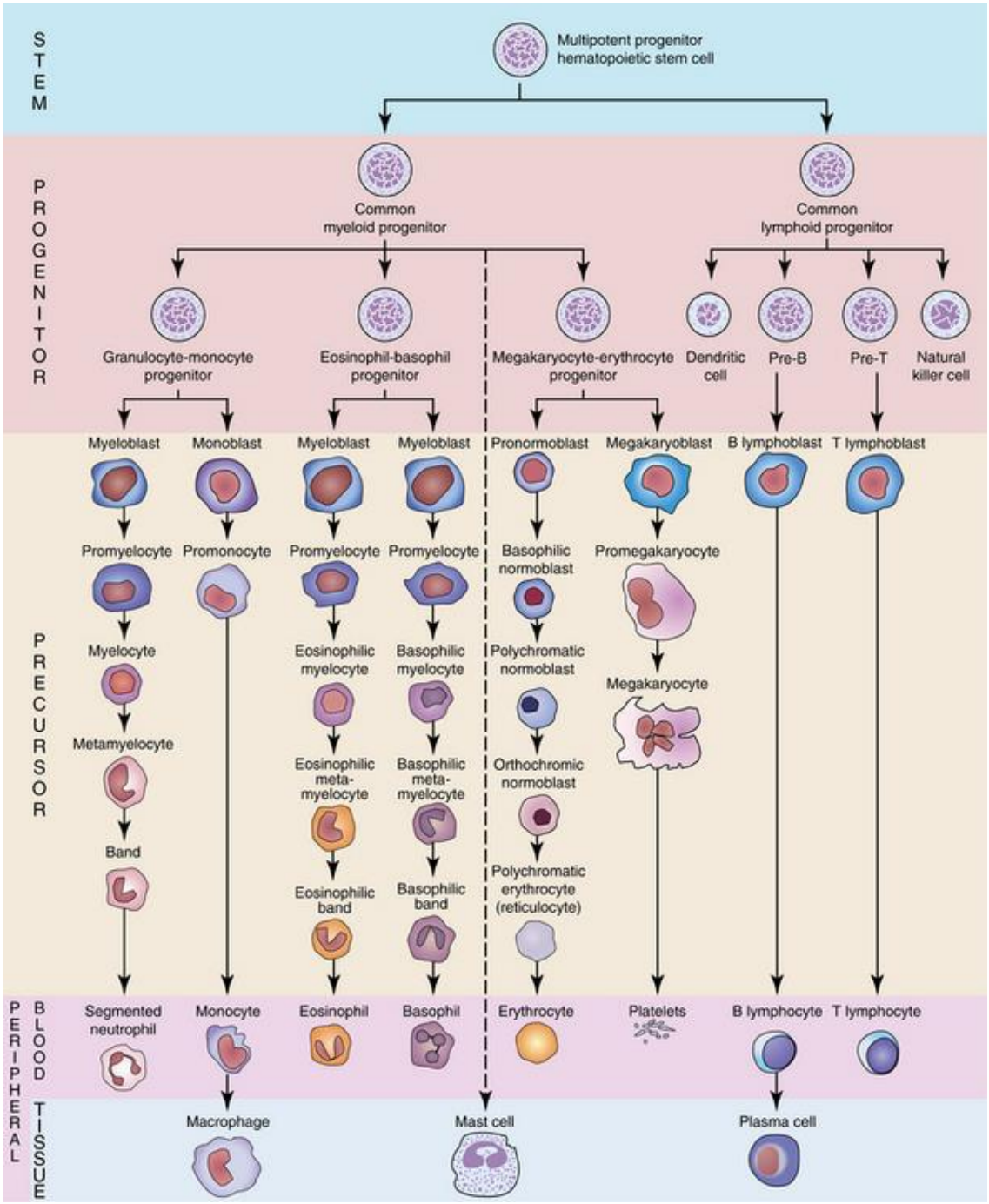
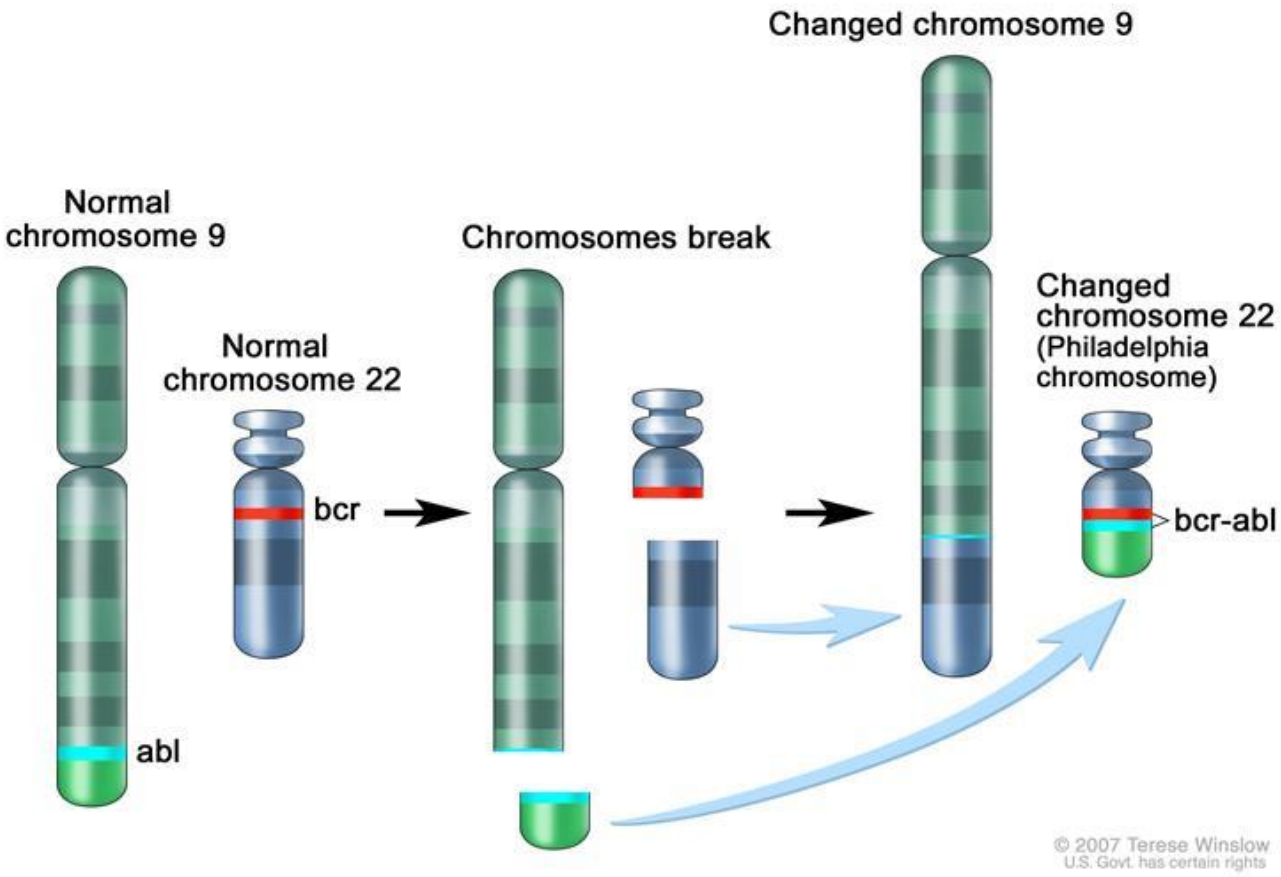
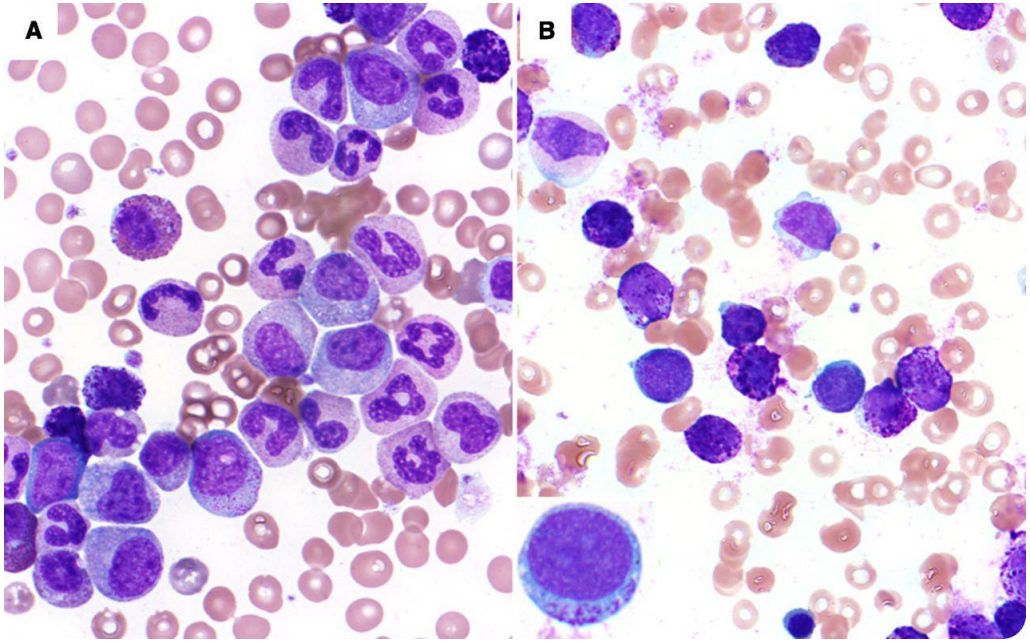
Chronic myeloid Leukemia

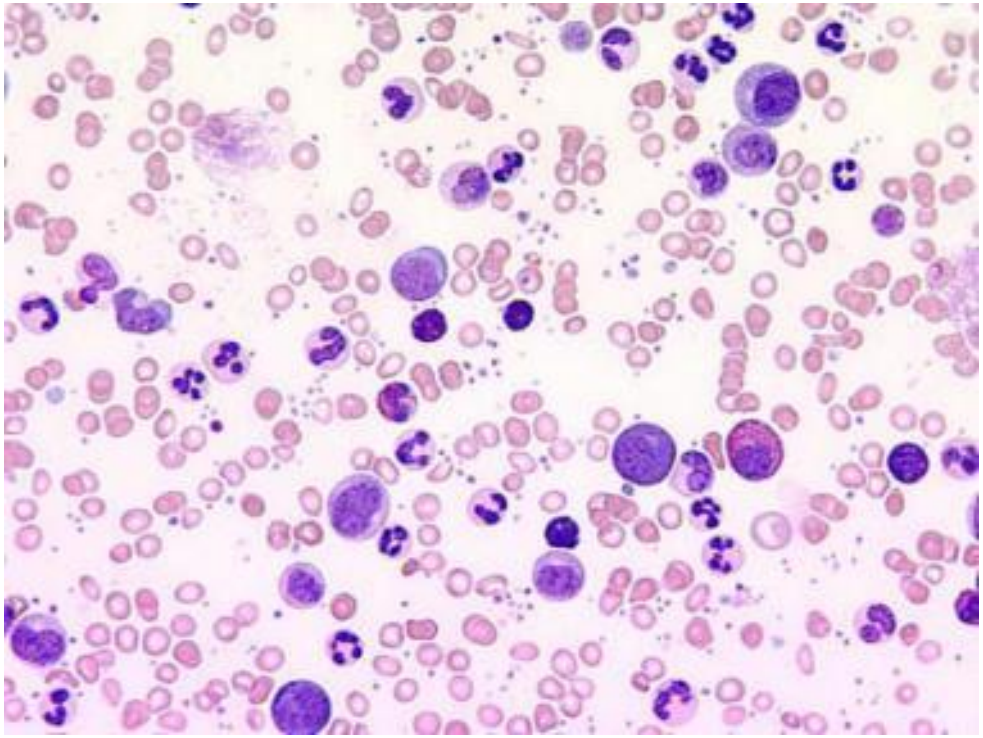


Hematopoesis

How and Why ?
Chromosomal TRANSLOCATION **t(9,22)**







BCR + ABL GENE

BCR-ABL Protein

Activates Tyrosine Kinases

Activates cellular division

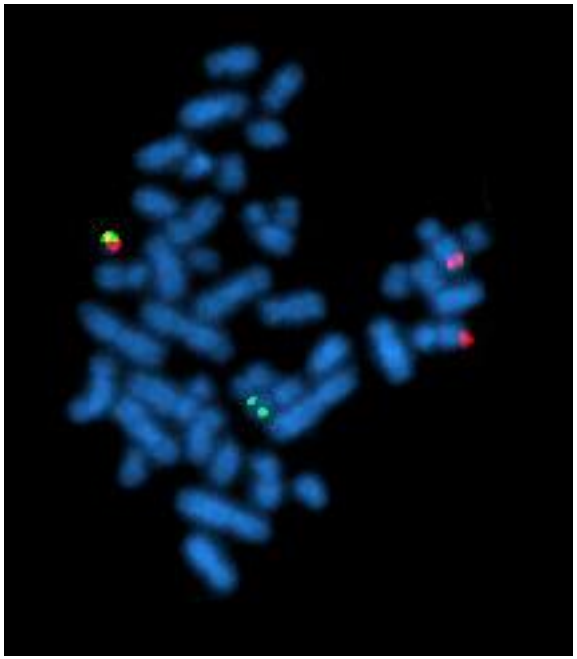
Cells devide too quickly!!!

Signs and Symptoms

- Discomfort or fullness in the upper left part of the abdomen, caused when the spleen and/or liver increases in size (hepato-**splenomegaly**)
- Recurrent **infections**
- Abnormal **bleeding**
- Fatigue and Malaise, or generally not feeling well
- Symptoms often called "B symptoms" that include fever, chills, night sweats, and weight loss

Diagnosis

1. CBC
2. Peripheral blood smear
3. Bone marrow analysis
4. **Molecular testing**
   - Cytogenetics and molecular biology
   - Fluorescence in situ hybridization (FISH)
     - Polymerase chain reaction (PCR)
5. Imaging tests: CT, MRI, Echography



The Phases

- **Chronic phase.**
  - less than 10% blasts.
  - 90% of people have chronic phase CML when they are diagnosed.
  - +/-symptoms go away once treatment begins.
- **Accelerated phase.**
  - 10% to 19% blasts in both the blood and bone marrow
  - Additional cytogenetic changes
- **Blast phase, also called blast crisis.**
  - 20% or more blasts in the blood or bone marrow
  - DD to AML – matureation phases of myeloid cells are present
  - often have a fever, an enlarged spleen, weight loss, and generally feel unwell.

Treatment

- tyrosine kinase inhibitors or TKIs
  - imatinib (Gleevec), dasatinib (Sprycel), nilotinib (Tasigna), bosutinib (Bosulif), and ponatinib (Iclusig).

1. **Hematologic remission** (normal complete blood cell count (CBC) and physical examination (no organomegaly)
2. **Cytogenetic remission** (normal chromosome returns with 0% Philadelphia chromosome–positive (Ph+) cells)
3. **Molecular remission** (negative polymerase chain reaction [PCR] result for the mutational BCR/ABL mRNA), which represents an attempt for cure and prolongation of patient survival

Treatment

- Chemotherapy
- Immunotherapy
- Stem cell transplantation/bone marrow transplantation

Clinical Presentation

39-year-old Female

- Housewife
- No toxic environment
- Non-smoker
- History of Gallbladder stones, External hemorrhoids and Hypertension gr II

The patient was admitted to the hospital showing asthenia, fatigue and pain in the left upper quadrant +-abdominal fullness

Findings

- Clinical examination
  - Massive Splenomegaly and hepatomegaly
- Laboratory findings
  - **CBC: WBC: 433.000 / mmc**; Promielocytes 10%; Neutrophil mielocytes 28%; Non-segmentated neutrophils 27% ; Segmentated neutrophils 20% ; Eo 5%; Ba 6%; Ly 4%; **Platelets: 446.000 / mmc** ; **Hb: 9 g / dl**;
  - **Bone marrow aspirate** - chronic myeloproliferative syndrome - type chronic myeloid leukemia
  - **Cytogenetic examination** : translocation t (9; 22) or Philadelphia chromosome, cytogenetic marker of the disease present in 100% of analyzed cells
  - **Molecular Biology Exam** : BCR - ABL major transcript detection - quantitative method : 100% present.

Treatment

- Hydroxyurea therapy at the dose of 6 tb / day (cytoreduction therapy).
- After 2 weeks the leukocytes decreased at 80.000 / mmc
- TKI - Tasigna (Nilotinib) was initiated : 600 mg/day
- At 6 months of treatment she achieved haematological, cytogenetic and molecular remission.
- **COMPLICATIONS:**

  At the start of Nilotinib treatment, she had a thrombocytopenia (65,000 / mmc) which required a temporary stop of treatment over a 2-week period during which the platelets turned normal and the treatment was resumed with the initial dose 600 mg / day

Thank you!