Pathology of the gingiva
**Periodontium:**

- Alveolar bone
- Cementum
- Gingiva or gums
- Periodontal ligament
Macroscopic features of gingiva

The gingiva is divided anatomically into marginal, attached and interdental areas.

Marginal gingiva
The marginal gingiva is the terminal edge of gingiva surrounding the teeth in collar like fashion. In about half of individuals, it is demarcated from the adjacent, attached gingiva by a shallow linear depression, the free gingival groove. Usually about 1 mm wide, it forms the soft tissue wall of the gingival sulcus. The marginal gingiva is supported and stabilized by the gingival fibers.

Attached gingiva
The attached gingiva is continuous with the marginal gingiva. It is firm, resilient, and tightly bound to the underlying periosteum of alveolar bone. The facial aspect of the attached gingiva extends to the relatively loose and movable alveolar mucosa, from which it is demarcated by the mucogingival junction. Attached gingiva may present with surface stippling.

Interdental gingiva
The interdental gingiva occupies the gingival embrasure, which is the interproximal space beneath the area of tooth contact. The interdental papilla can be pyramidal or have a "col" shape. Attached gingiva is resistant to masticatory forces and always keratinised.
A unique structure that binds the gingiva to the dental surface.

Junctional epithelium (connective tissue under the epithelium of the gingiva)

Apicocoronal length: 2 mm

Width:
- apical: only several cell layer
- coronal: 15-30 cell layer
- at the bottom of the sulcus: 0,15 mm
circular, around the tooth neck (free margin); dentogingival fibers, ;transseptali fibers, between teeth; septogingival fibers, between interdental septum and interdental papilla.
Risk factors for periodontal disease:

- Diabetes mellitus
- Pregnancy and sex hormones
- Nutrition
- Hematological diseases
- Drugs
- Immunsuppression (AIDS)
- Smoking

PATHOGENESIS

<table>
<thead>
<tr>
<th>Microbial plaque</th>
<th>Host defense</th>
</tr>
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<tbody>
<tr>
<td>Direct injury</td>
<td>Salivary factors</td>
</tr>
<tr>
<td>Toxic products</td>
<td>Crevicular fluid</td>
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<tr>
<td>Enzymes</td>
<td>Epithelial barrier</td>
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<tr>
<td>Antigenic challenge</td>
<td>Migrating neutrophils</td>
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<tr>
<td></td>
<td>Immune response</td>
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<td></td>
<td>Tissue regeneration</td>
</tr>
</tbody>
</table>
Dental deposits:
- acquired pellicle (glycoproteins)
- dentogingival plaque
- mineralized plaque
- debris
1. Gingival Diseases
   A. Dental plaque-induced gingival diseases*
      1. Gingivitis associated with dental plaque only
         a. without other local contributing factors
         b. with local contributing factors (See VIII A)
      2. Gingival diseases modified by systemic factors
         a. associated with the endocrine system
            1) puberty-associated gingivitis
            2) menstrual cycle-associated gingivitis
            3) pregnancy-associated
               a) gingivitis
               b) pyogenic granuloma
            4) diabetes mellitus-associated gingivitis
            b. associated with blood dyscrasias
               1) leukemia-associated gingivitis
               2) other
      3. Gingival diseases modified by medications
         a. drug-influenced gingival diseases
            1) drug-influenced gingival enlargements
            2) drug-influenced gingivitis
               a) oral contraceptive-associated gingivitis
               b) other
         b. allergic reactions
            1) dental restorative materials
               a) mercury
               b) nickel
               c) acrylic
               d) other
            2) reactions attributable to
               a) toothpastes/dentifrices
               b) mouthrinses/mouthwashes
               c) chewing gum additives
               d) foods and additives
            3) other
      4. Gingival diseases modified by malnutrition
         a. ascorbic acid-deficiency gingivitis
         b. other
   B. Non-plaque-induced gingival lesions
      1. Gingival diseases of specific bacterial origin
         a. Neisseria gonorrhoea-associated lesions
         b. Treponema pallidum-associated lesions
         c. streptococcal species-associated lesions
         d. other
      2. Gingival diseases of viral origin
         a. herpesvirus infections
            1) primary herpetic gingivostomatitis
            2) recurrent oral herpes
            3) varicella-zoster infections
         b. other
      3. Gingival diseases of fungal origin
         a. Candida-species infections
            1) generalized gingival candidosis
            b. linear gingival erythema
            c. histoplasmosis
            d. other
      4. Gingival lesions of genetic origin
         a. hereditary gingival fibromatosis
         b. other
      5. Gingival manifestations of systemic conditions
         a. mucocutaneous disorders
            1) lichen planus
            2) pemphigoid
            3) pemphigus vulgaris
            4) erythema multiforme
            5) lupus erythematosus
            6) drug-induced
            7) other
         b. allergic reactions
            1) dental restorative materials
               a) mercury
               b) nickel
               c) acrylic
               d) other
            2) reactions attributable to
               a) toothpastes/dentifrices
               b) mouthrinses/mouthwashes
               c) chewing gum additives
               d) foods and additives
            3) other
      6. Traumatic lesions (factitious, iatrogenic, accidental)
         a. chemical injury
         b. physical injury
         c. thermal injury
      7. Foreign body reactions
      8. Not otherwise specified (NOS)
<table>
<thead>
<tr>
<th>II. Chronic Periodontitis†</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Localized</td>
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<tr>
<td>B. Generalized</td>
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<tr>
<th>III. Aggressive Periodontitis†</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Localized</td>
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<tr>
<td>B. Generalized</td>
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<tr>
<th>IV. Periodontitis as a Manifestation of Systemic Diseases</th>
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</thead>
<tbody>
<tr>
<td>A. Associated with hematological disorders</td>
</tr>
<tr>
<td>1. Acquired neutropenia</td>
</tr>
<tr>
<td>2. Leukemias</td>
</tr>
<tr>
<td>3. Other</td>
</tr>
<tr>
<td>B. Associated with genetic disorders</td>
</tr>
<tr>
<td>1. Familial and cyclic neutropenia</td>
</tr>
<tr>
<td>2. Down syndrome</td>
</tr>
<tr>
<td>3. Leukocyte adhesion deficiency syndromes</td>
</tr>
<tr>
<td>4. Papillon-Lefèvre syndrome</td>
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<td>5. Chediak-Higashi syndrome</td>
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<td>6. Histiocytosis syndromes</td>
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<td>7. Glycogen storage disease</td>
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<td>8. Infantile genetic agranulocytosis</td>
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<td>9. Cohen syndrome</td>
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<tr>
<td>10. Ehlers-Danlos syndrome (Types IV and VIII)</td>
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<td>11. Hypophosphatasia</td>
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<tr>
<td>12. Other</td>
</tr>
<tr>
<td>C. Not otherwise specified (NOS)</td>
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<table>
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<tr>
<th>V. Necrotizing Periodontal Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Necrotizing ulcerative gingivitis (NUG)</td>
</tr>
<tr>
<td>B. Necrotizing ulcerative periodontitis (NUP)</td>
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</table>

<table>
<thead>
<tr>
<th>VI. Abscesses of the Periodontium</th>
</tr>
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<tbody>
<tr>
<td>A. Gingival abscess</td>
</tr>
<tr>
<td>B. Periodontal abscess</td>
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<tr>
<td>C. Pericoronal abscess</td>
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<thead>
<tr>
<th>VII. Periodontitis Associated With Endodontic Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Combined periodontic-endodontic lesions</td>
</tr>
<tr>
<td>B. Localized tooth-related factors that modify or predispose to plaque-induced gingival diseases/periodontitis</td>
</tr>
<tr>
<td>1. Tooth anatomic factors</td>
</tr>
<tr>
<td>2. Dental restorations/appliances</td>
</tr>
<tr>
<td>3. Root fractures</td>
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<tr>
<td>4. Cervical root resorption and cemental tears</td>
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</tbody>
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<table>
<thead>
<tr>
<th>VIII. Developmental or Acquired Deformities and Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Localized tooth-related factors that modify or predispose to plaque-induced gingival diseases/periodontitis</td>
</tr>
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<td>1. Tooth anatomic factors</td>
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<thead>
<tr>
<th>C. Mucogingival deformities and conditions around teeth</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Gingival/soft tissue recession</td>
</tr>
<tr>
<td>a. facial or lingual surfaces</td>
</tr>
<tr>
<td>b. interproximal (papillary)</td>
</tr>
<tr>
<td>2. Lack of keratinized gingiva</td>
</tr>
<tr>
<td>3. Decreased vestibular depth</td>
</tr>
<tr>
<td>4. Aberrant frenum/muscle position</td>
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<tr>
<td>5. Gingival excess</td>
</tr>
<tr>
<td>a. pseudopocket</td>
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<tr>
<td>b. inconsistent gingival margin</td>
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<tr>
<td>c. excessive gingival display</td>
</tr>
<tr>
<td>d. gingival enlargement (See I.A.3. and I.B.4.)</td>
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<tr>
<td>6. Abnormal color</td>
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<tr>
<th>D. Occlusal trauma</th>
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</thead>
<tbody>
<tr>
<td>1. Primary occlusal trauma</td>
</tr>
<tr>
<td>2. Secondary occlusal trauma</td>
</tr>
</tbody>
</table>
Initial gingivitis
   cellular exudate (enhanced migration of neutrophils)
   fluid exudate (increased crevicular fluid flow)

Early gingivitis
   lymphocytic infiltration
   impaired barrier function of the junctional epithelium
   gingival pocket formation, subgingival plaque

Established gingivitis
   expansion of the inflamed area, destruction of gingival connective tissue
   plasmacell infiltrate
   deepening of the gingival pocket, thinning of epithelium
I) Gingival disease
   A) Dental plaque induced
      1) Gingivitis associated with dental plaque only
         Example: BLEEDING ON PROBING (BoP)

One of the earliest signs of gingivitis is bleeding on probing.
Gingivitis simplex

Grade 0 Free of inflammation
Gingivitis simplex
Grade 1

Mild superficial changes and color changes
Gingivitis simplex

Grade 2

Edema, swelling, bleeding on probing
Grade 3. Erythema, swelling, spontaneous bleeding, ulceration
A) Dental plaque induced
   2) Gingival diseases modified by systemic factors
      a) Associated with endocrine system

The gingival tissues may have a modified reaction to dental plaque with changes in circulating estrogen and progesterone levels.

These changes result in the inflammation having more vascular components and this is generally not very obvious in puberty or with menstrual cycles but can be quite pronounced in some pregnant patients.
A) Dental plaque induced
  2) Gingival diseases modified by systemic factors
     a) Associated with endocrine system
  3) PREGNANCY GINGIVITIS

Intense burgundy color and marked gingival hypertrophy.

These lesions bleed profusely.
A) Dental plaque induced
   2) Gingival disease modified by systemic factors
      a) Associated with endocrine system
         4) DIABETES MELLITUS ASSOCIATED GINGIVITIS

Marked inflammatory reaction and hypertrophy of the free gingiva.

This reflects an increased gingival reaction to plaque with consequent increased risk of periodontal disease.
PERIODONTAL ABSCESS

A) Dental plaque induced
2) Gingival disease modified by systemic factors
   a) Associated with endocrine system
   4) DIABETES MELLITUS ASSOCIATED
A) Dental plaque induced
   2) Gingival disease modified by systemic factors
      b) Associated with blood dyscrasias
         1) LEUKEMIA ASSOCIATED GINGIVITIS

Intragingival hemorrhagia
A) Dental plaque induced
   3) Gingival diseases modified by medications
      a) Drug induced gingival disease
         1) PHENYTOIN GINGIVAL HYPERThROPHY

Epithelial and connective tissue hyperplasia, with secondary Inflammation.
A) Dental plaque induced
   3) Gingival diseases modified by medications
      a) Drug induced gingival disease
         1) CALCium CHANNEL BLOCKERS - NIFEDIPINE

10-15% of the patient show gingival hyperplasia.
A) Dental plaque induced
3) Gingival diseases modified by malnutrition
   a) ASCORBIC ACID GINGIVITIS

This gingivitis seen only in the late stages of scurvy is plaque associated. Severe vitamin C deficiency induces absence of intracellular oxidation, abnormal collagen formation, gingival hypertrophy with hemorrhage and mucosal echymoses.
B) Non plaque induced
   1) Gingival diseases of specific bacterial origin
      Example: RECURRENT APHTOUS STOMATITIS

Recurrent aphtous stomatitis is divided in aphthous minor, aphthous major and herpetiform ulcers. Aphthous minor rarely affects the gingiva. These ulcers are very painful and may last up to 14 days. Etiolgy is unknown.
Symptoms:
Sores on the inside of the cheeks or gums:
   Fever
   General discomfort, uneasiness, or ill feeling
   Very sore mouth with no desire to eat
   Bad breath

Herpetic gingivostomatitis

A combination of gingivitis and stomatitis, or an inflammation of the oral mucosa and gingiva in the younger adults, infants.

HSV-1!!

Symptoms:
Sores on the inside of the cheeks or gums:
   Fever
   General discomfort, uneasiness, or ill feeling
   Very sore mouth with no desire to eat
   Bad breath
B) Non plaque induced
   2) Gingival diseases of viral origin
      a) Herpes virus - PRIMARY HERPETIC GINGIVOSTOMATITIS (PHGS)

**Gingivostomatitis herpetica**

Gingival haemorrhage and ulcers, that are preceded by vesicle formations. Later sero-purulent exudate.
The intraoral lesions of RHS are characterized by small linear vesicles that rupture and leave small areas of ulceration. Both the free and attached gingiva can be the site of these lesions.
B) Non plaque induced

2) Gingival diseases of viral origin
   a) Herpes virus - AIDS RELATED KAPOSI SARCOMA

KAPOSI SARCOMA – HHV8
Mimics pyogen granuloma !!!
B) Non plaque induced
   3) Gingival diseases of fungal origin
      a) Candida species infections
         1) GENERALIZED GINGIVAL CANDIDIASIS
II) Chronic Periodontitis
2) Generalized
IV) Periodontitis as a Manifestation of Systemic Disease
   A) Associated with hematologic disorders
Acute necrotizing ulcerative gingivitis (ANUG)

Necrotizing periodontal disease is caused by a bacterial infection that includes anaerobes such as P. intermedia and Fusobacterium as well as spirochetes, such as Borrelia and Treponema.

Symptoms:
- necrosis and/or punched out ulceration of the interdental papillae ("punched-out papillae") or gingival margin
- pseudomembranous formation
- painful, bright red marginal gingiva that bleed upon gentle manipulation
- halitosis
Nodular lesions on the gingiva
GINGIVAL NODULES/MASSES

- Reactive/inflammatory gingival nodules, solitary or diffuse
- Peripheral (extraosseous) odontogenic cysts and tumors
- Soft tissue tumors (such as nerve sheath or smooth muscle tumors)
- Extension of intrabony lesions into the gingiva
- Metastatic tumors to the gingiva
Fibroma (fibrovascular hyperplasia/polyp)

Nodule of fibrous tissue with scattered vessels and variable edema and inflammation; crevicular epithelium with underlying plasma cells often seen.
PYOGEN GRANULOMA

This type of epulis is neither pyogenic nor a true granuloma, but it is a vascular lesion. About 75% of all pyogenic granulomas occur on the gingiva.

- Polypoid capillary hemangiomma, ulcerating, after microtraumatisation
- Proliferating capillaries, oedema, inflammatory infiltrate

Pyogenic granuloma is considered to be an exuberant response to a chronic mild irritant. Its clinical appearance is similar to that seen in pregnancy gingivitis but generally confined to a single area. Pyogenic granulomas also bleed easily because they contain multiple capillaries.

**Granuloma gravidarum**

- Pyogen granuloma variant

Also termed a "pregnancy tumor" or "granuloma gravidarum," this lesion is identical to a pyogenic granuloma in all respects apart from the fact that it occurs exclusively in pregnant females.

- Pyogen granuloma variant
- Pregnant women: 1-5%; gingival node;
PYOGEN GRANULOMA

Chronic, mild irritation
PYOGEN GRANULOMA
**Epulis**
Epulis (plural epulides) is any benign tumor (i.e. lump) situated on the gingival or alveolar mucosa.

**Giant cell epulis**
This epulis contains giant cells. It is also termed peripheral giant cell granuloma. It appears in the mouth as an overgrowth of tissue due to irritation or trauma.
Abb. 2-1  Fibröse Epulis mit kleiner, traumabedingter Ulzeration zwischen Zahn 45 und 47.

Abb. 2-3  Große fibröse Epulis im rechten Oberkiefer.

Abb. 2-2  Röntgenologisch findet sich eine schüsselförmige Erosion im betroffenen Bereich.

Abb. 2-4  Ausgedehnte fibröse Epulis im Bereich des rechten Unterkiefers.
PYOGEN GRANULOMA
Disorders of the hemopoietetic system

I. Myeloid diseases
Differentiation of hemopoetic system

Pathology of hemopoetic system

Stem Cell

Multipotent progenitor

Committed progenitor

Mature cells

HSC

MPP

CFU-GEMM

CFU-GE

BFU-E

CFU-meg

CFU-E

Megakaryocyte

Erythrocyte

Platelets

Myeloid

CMP

CFU-G

CFU-Eo

CFU-Baso

Neutrophil

Basophil

B Cell

T Cell

NK Cell

Lymphoid

CLP

Pro-B

Pro-T

Macrophage

Dendritic Cell

Osteoclast
Benign diseases

Reactive granulocytosis – monocytosis: infections, diseases with necrosis

Neutropenia: congenital, idiopathic, different drugs (aminopyrine), infections, aplastic anemia, bone marrow infiltration

agranulocytosis:
neutrophil count < 500 / μl
life threatening infections

Chronic granulomatous disease:
NADPH oxidase defects
in neutrophil granulocytes
Myeloid neoplasms
Classification

Acute myeloid leukemia - with recurrent cytogenetic abnormalities
- with multilineage dysplasia
- chemotherapy related
- not otherwise classified, FAB

Chronic myeloproliferative diseases - CML
- PRV
- ET
- CIMF

Myelodysplastic syndromes

Myeloproliferative / myelodysplastic diseases
Pathology of hemopoetic system

Diagnosis I.

**DIAGNOSIS OF HEMOPOIETIC SYSTEM**

- morphology
- immunophenotype
- genotype

**CLINICAL DATA**

- Blood smear
- Bone marrow smear
- Bone marrow biopsy
- Bone marrow cytogenetics
- Immunophenotype
- Flow cytometry
- Cytogenetic metaphase
- FISH
- Molecular data
Cytogenetics

Metaphase (banding) cytogenetics: complete karyotype from dividing cells (analyzing 20-50 cells)

Metaphase FISH – specific, 20 cells

Interphase FISH, specific, 200 cells

Metaphase multicolor FISH, complete karyotype + specific
Acute myeloid leukemia

In the bone marrow > 20 % myeloid blasts + / - leukemic periph. blood picture

Blast: myeloid precursor with maturation arrest, showing myeloid stem cell-, granulopoetic-, monocytic-, erythroid- and megakaryocytic markers: CD34, CD117, MPO, CD13, CD33, CD15, CD14, CD36, CD61, glycophorin +

Classification: by cytogenetics, etiology, maturation

promyelocytic leukemia t(15;17), PML-RARα, abnormal retinoic acid receptor, maturation defect
Acute leukemia

Symptoms, pathology: blastosis → bone marrow failure

Blastosis – microcirculation disorders, leukostasis, infiltration of organs

Granulocytopenia – infections

Thrombocytopenia – bleeding

Gingival hyperplasia – monocytic AL
Acute leukemia – causes of death

Secunder aplasia
Bleeding
Infections - bacterial fungal sepsis generalized virus
Diffuse alveolar damage
Toxic kidney, liver insuff.
Leukostasis
Multiorgan failure

ARDS
cholestasis
Invasive fungal (mucor) pneumonia and carditis
Generalized herpes zoster
Invasive candidiasis
Absceding bacterial pneumonia
Myelodysplastic syndromes (MDS)

Definition: Clonal neoplastic proliferation of bone marrow (BM) multipotent stem cells with peripheral single or multi-lineage cytopenia.
- maturation defects, ineffective hematopoiesis, blast count < 20%
- chromosomes: isolated and complex aberrations of 5, 7, 8, 20

Elderly, chronic disease, substitution refractor anaemia, granulocytopenia, thrombocytopenia, pancytopenia, weekness, infections, bleeding

RA, RARS erythrodysplasia, anemia, BM blast < 5%, course of disease is prolonged, cause of death: infections, siderosis

RCMD dysplasia of at least 2 cell lineages, pancytopenia, blast < 5%, bone marrow insufficiency, or transformation into AML

RAEB dysplasia of at least 2 cell lineages, pancytopenia, blast 5–20%, transformation into AML
# Chronic myeloproliferative diseases

<table>
<thead>
<tr>
<th>Chronic myeloid leukemia</th>
<th>Polycythemia rubra vera</th>
<th>Essential thrombocytopenia</th>
<th>Idiopathic myelofibrosis</th>
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</thead>
<tbody>
<tr>
<td>Definition: clonal, malignant disease of bone marrow with hypercellular, hyperplastic effective hematopoiesis producing elevated cell counts of one or more cell lineages in the peripheral blood.</td>
<td>Granulocytic hyperplasia</td>
<td>Erythroid hyperplasia</td>
<td>Megakaryocytic hyperplasia</td>
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<tr>
<td>Leukocytosis organomegaly</td>
<td>Polyglobulia</td>
<td>thombosis bleeding</td>
<td>Extramedullary hematopoiesis, organomegaly</td>
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<tr>
<td>Bcr/abl translocation t(9;22)</td>
<td>Jak-2 mutation 90%</td>
<td>Jak-2 mutation Calreticulin mut. MPL mut.</td>
<td>Jak-2 mutation Calreticulin mut. MPL mut.</td>
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<tr>
<td>Bone marrow insufficiency, BM fibrosis, extramedullary hematopoiesis / blastic crisis</td>
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