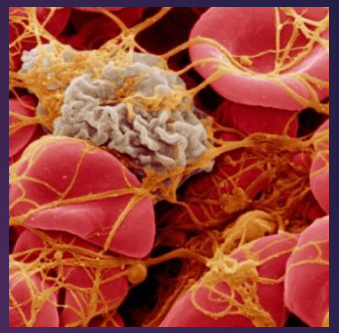
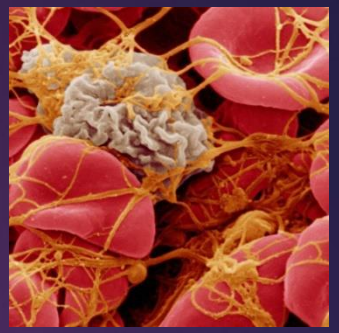


COAGULOPATIA DE CONSUMO EN LEUCEMIAS AGUDAS

SUSANA CALDERÓN AEDO

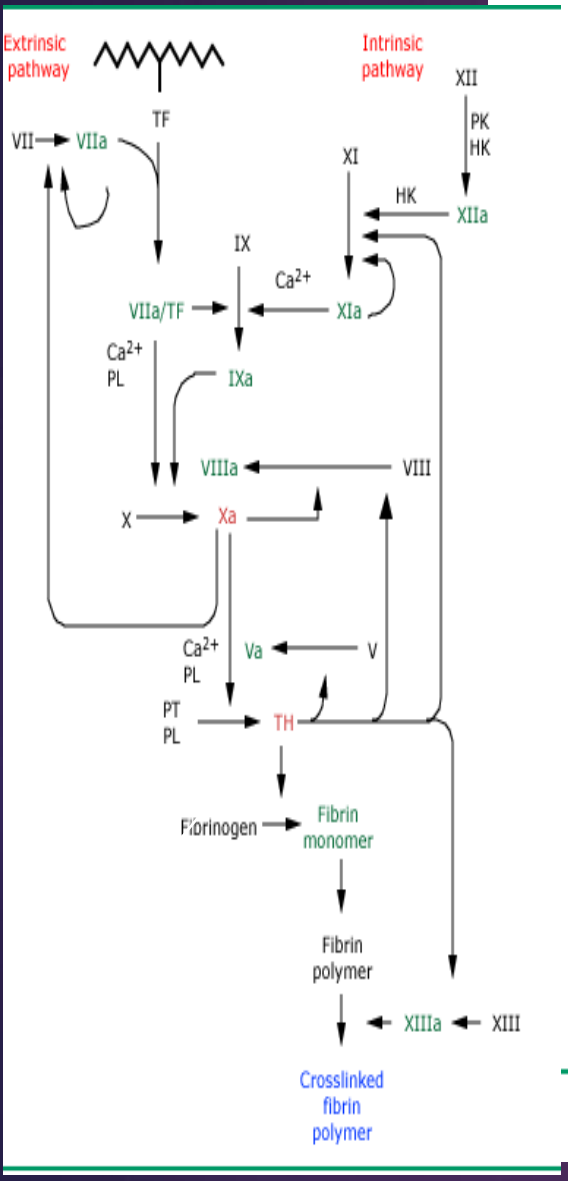
MEDICINA INTERNA-HEMATOLOGÍA

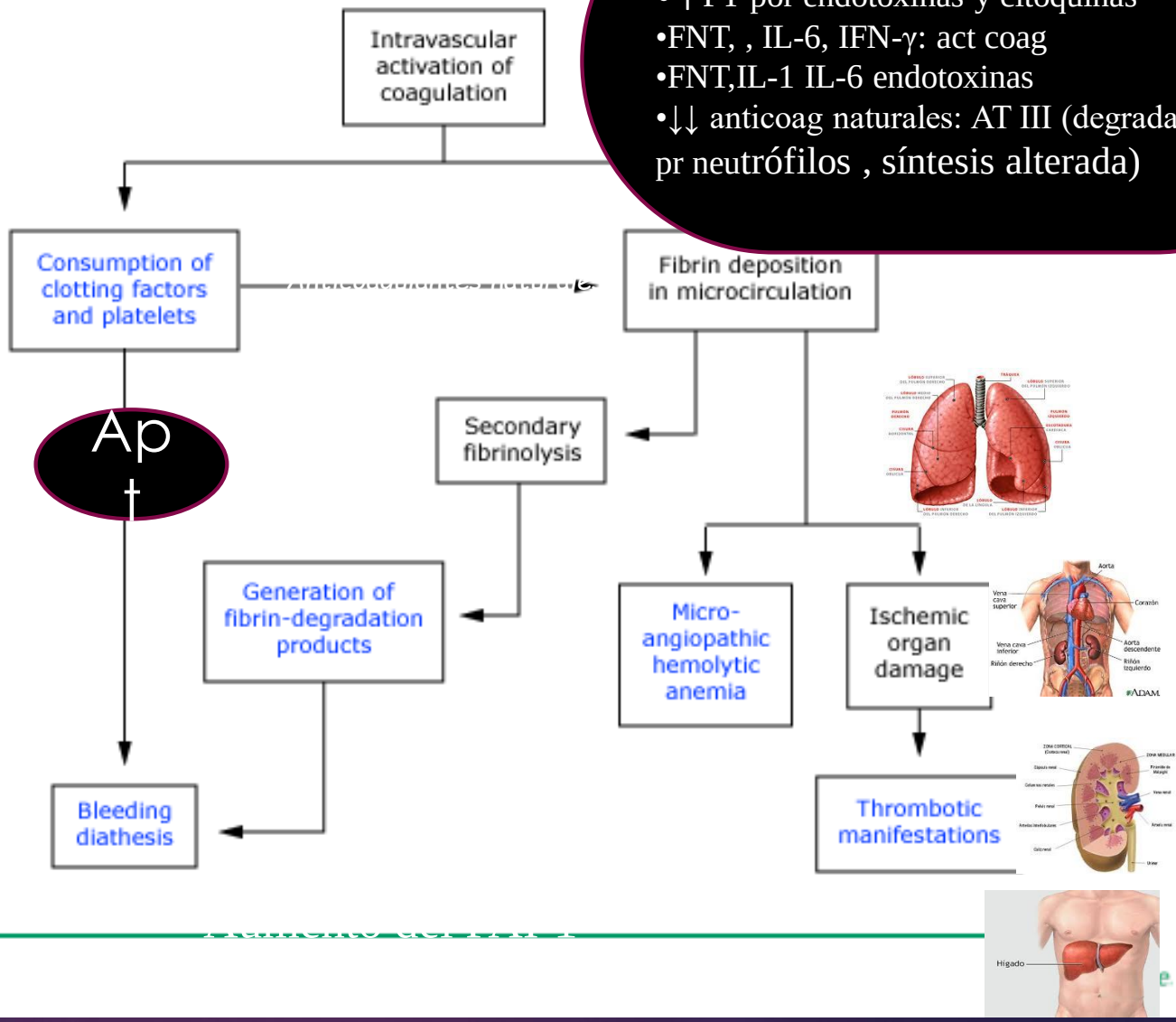
COAGULOPATIA DE CONSUMO EN LEUCEMIAS AGUDAS



- CID
- LEUCEMIAS CLASIFICACION
- LEUCEMIA PROMIELOCITICA
- Epidemiologia
- Clínica
- Laboratorio
- Manejo
- Conclusiones

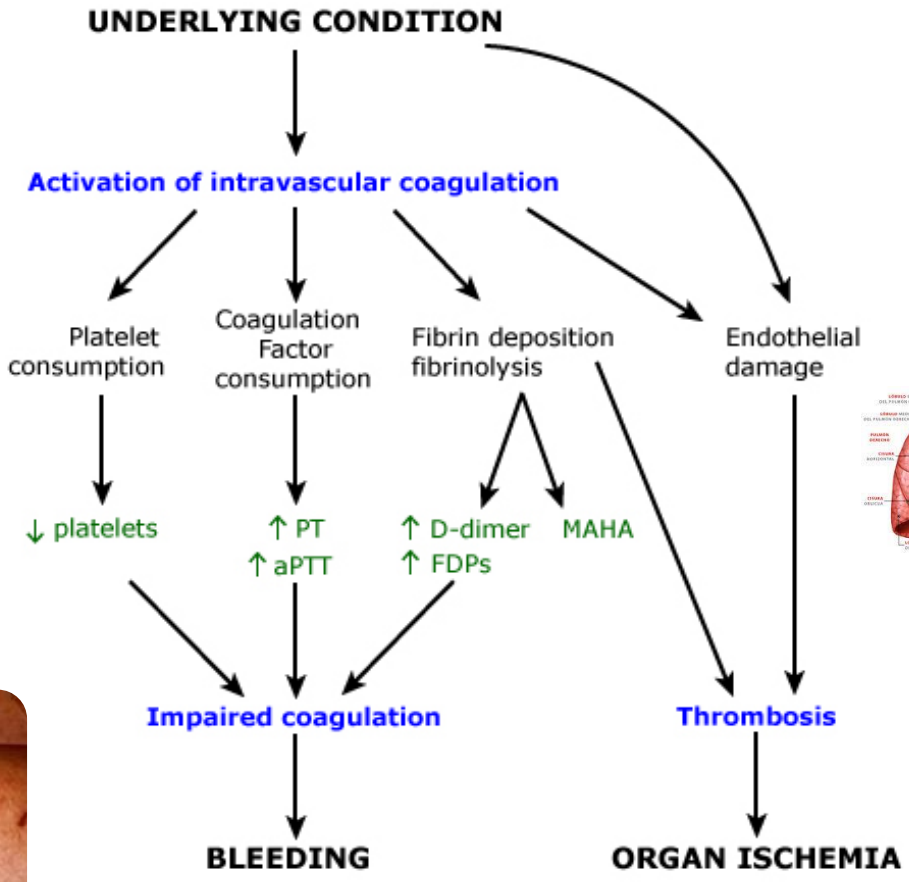
Pathophysiology of the clinical manifestati… intravascular coagulation

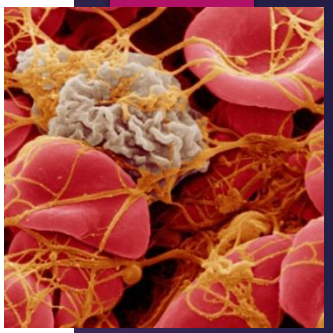


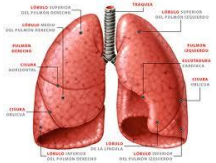


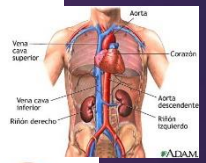
- Entrada de FT
- Daño endotelio : FT
- ↑FT por endotoxinas y citoquinas
- FNT, , IL-6, IFN-γ: act coag
- FNT,IL-1 IL-6 endotoxinas
- ↓↓ anticoag naturales: AT III (degrada pr neutrófilos , síntesis alterada)

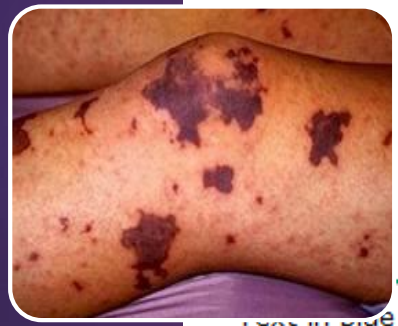
Pathogenesis of disseminated intravascular coagulation

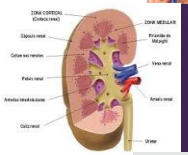


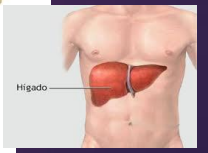












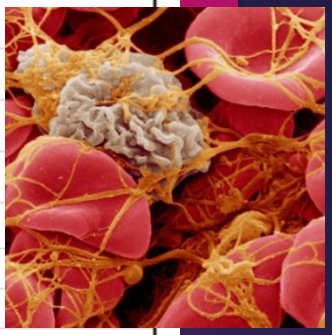
Text in blue refers to pathophysiologic processes; text in green denotes associated laboratory abnormalities. Refer to UpToDate topics on disseminated intravascular coagulation for additional details.

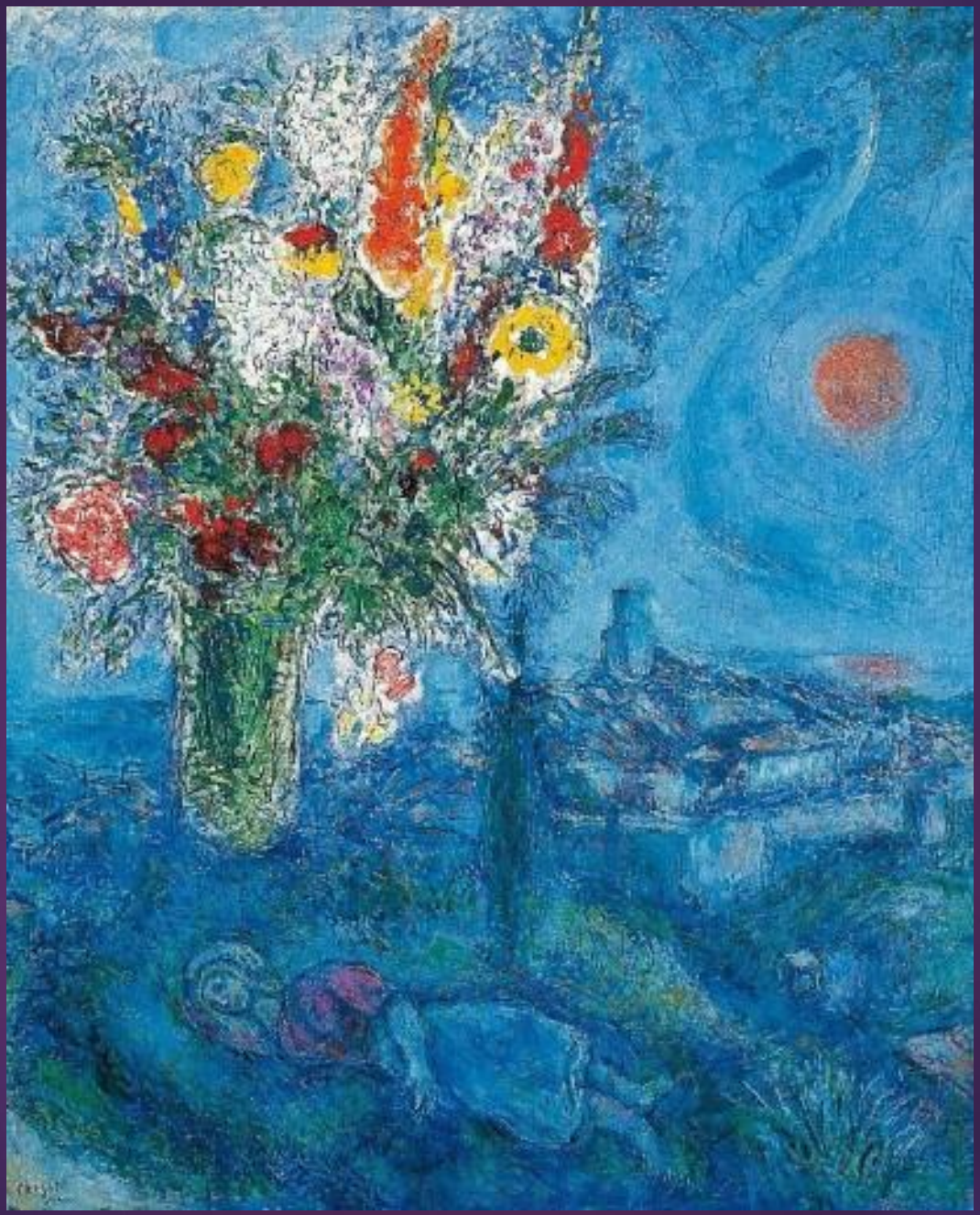
PT: prothrombin time; aPTT: activated partial thromboplastin time; FDPs: fibrin degradation products; MAHA: microangiopathic hemolytic anemia.

UpToDate®

Major causes of disseminated intravascular coagulation

Events that initiate DIC
Septicemia - Gram negative and Gram positive
Crush injury or complicated surgery
Severe head injury
Cancer procoagulant (Trousseau's syndrome)
Acute leukemia, especially promyelocytic
Complications of pregnancy
Amniotic fluid embolism
Abruptio placentae
HELLP syndrome
Eclampsia and severe preeclampsia
Septic abortion
Amphetamine overdose
Giant hemangioma (Kasabach-Merritt syndrome)
Abdominal aortic aneurysm
Peritoneovenous shunt
Acute hemolytic transfusion reaction (ABO incompatibility)
Paroxysmal nocturnal hemoglobinuria
Snake and viper venoms
Liver disease
Fulminant hepatic failure
Reperfusion after liver transplantation
Heat stroke
Burns
Purpura fulminans
Events that complicate and propagate DIC
Shock
Complement pathway activation





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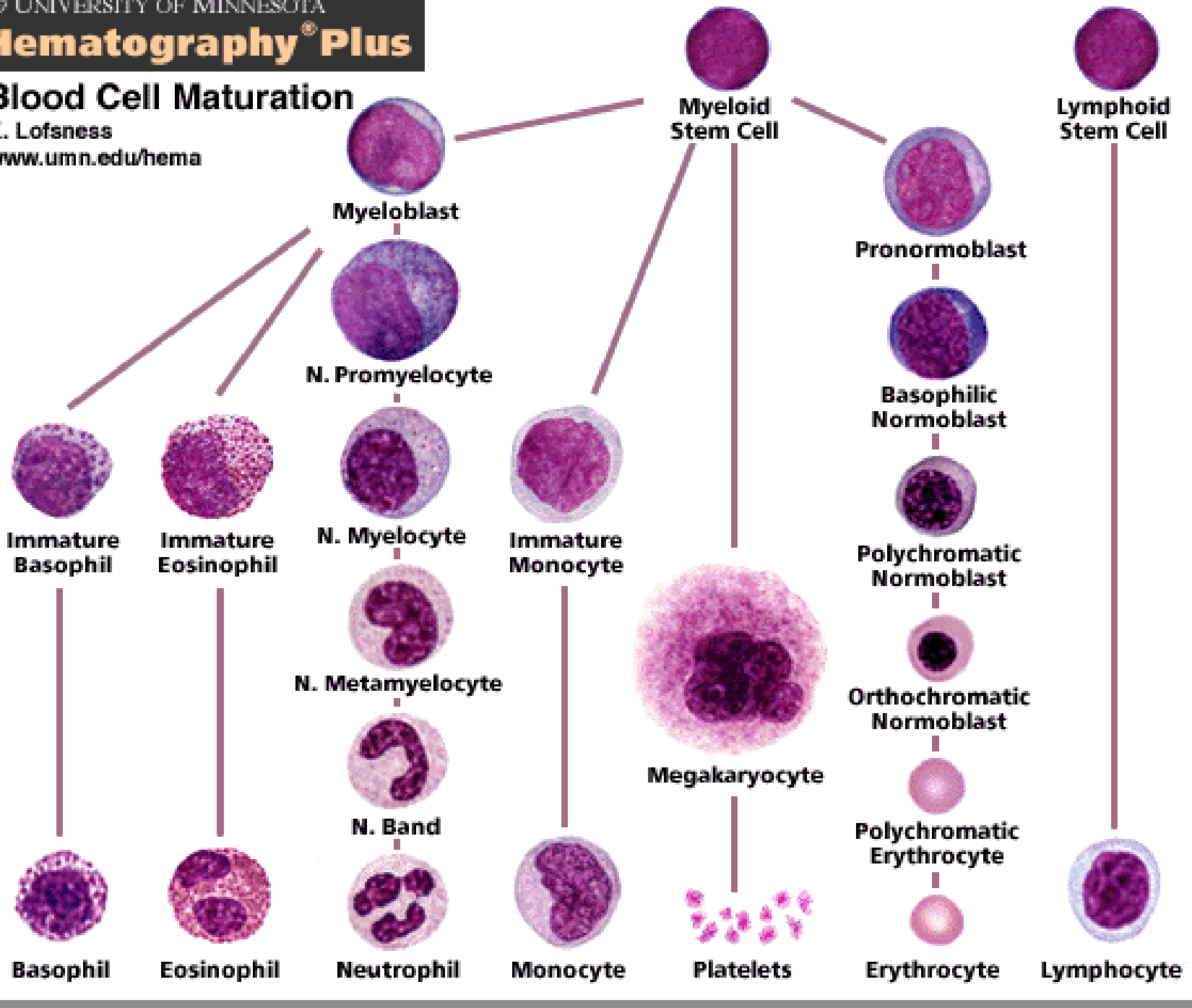
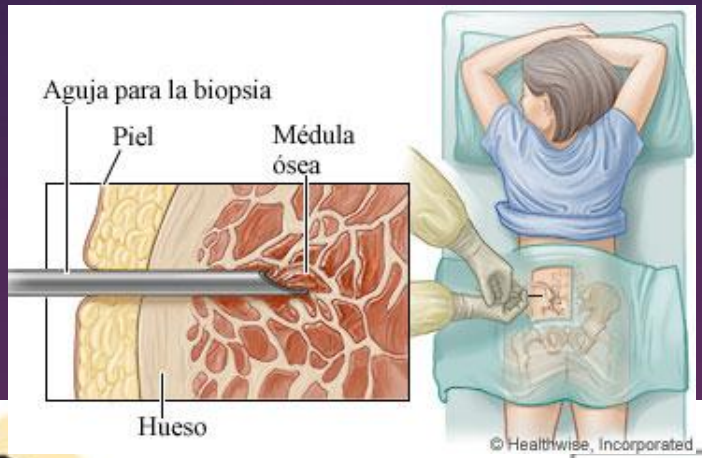
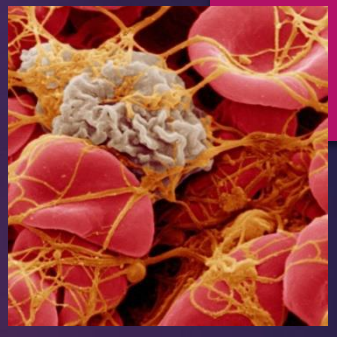
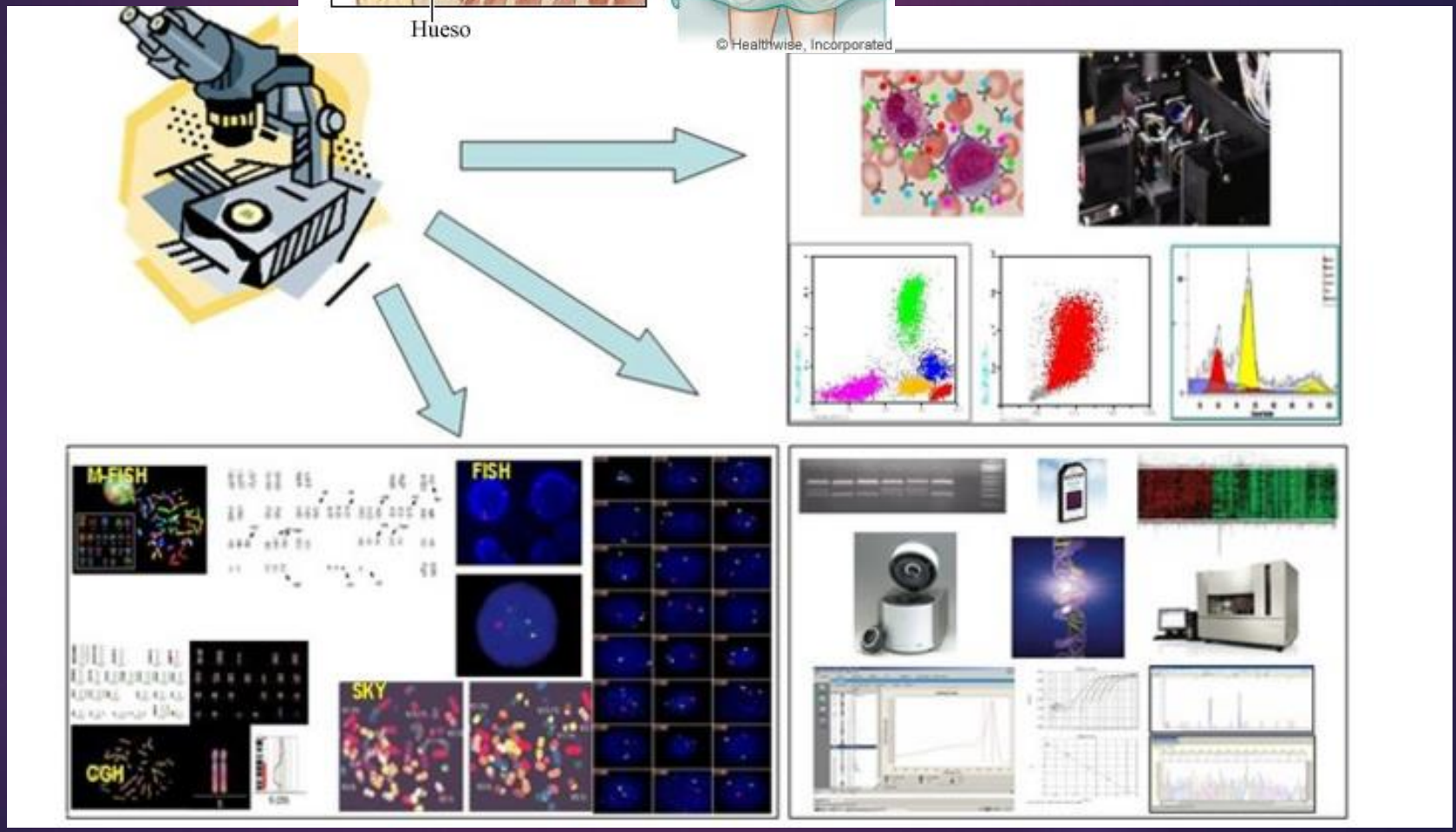
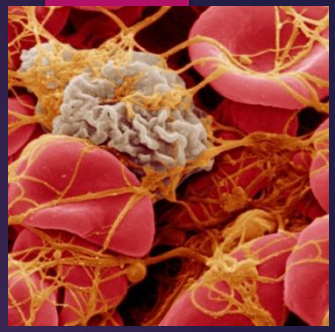


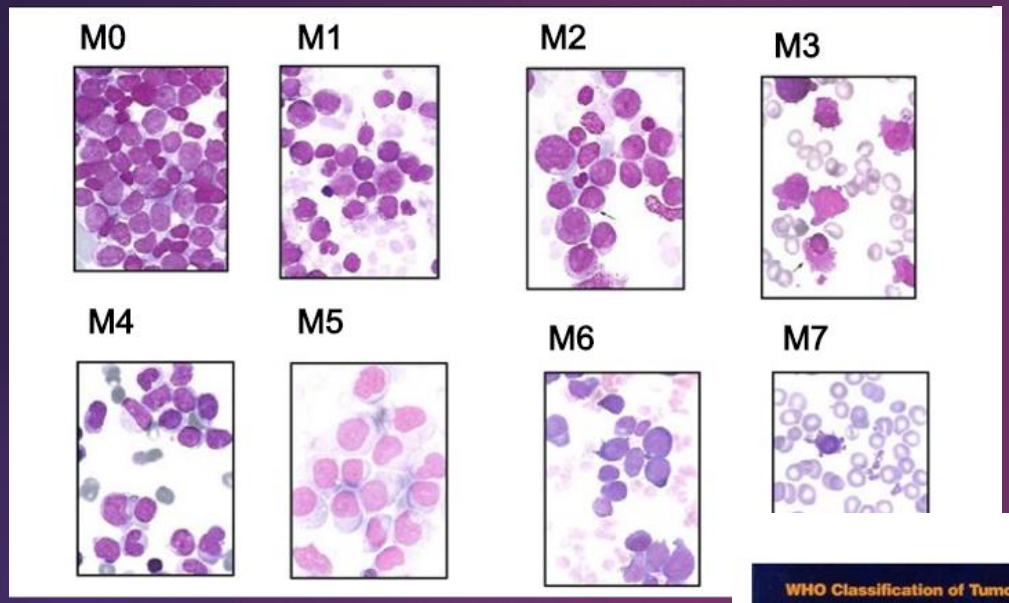






LEUCEMIAS MIELOIDES CLASIFICACION FAB y OMS





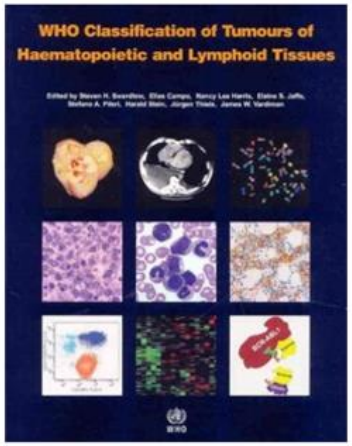


Table 1.07 Acute myeloid leukaemia and related myeloid neoplasms.

Acute myeloid leukaemia with recurrent genetic abnormalities
- AML with t(8;21)(q22;q22); *RUNX1-RUNX1T1*
- AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22); *CBFB-MYH11*
- APL with t(15;17)(q22;q12); *PML-RARA*
- AML with t(9;11)(p22;q23); *MLLT3-MLL*
- AML with t(6;9)(p23;q34); *DEK-NUP214*
- AML with inv(3)(q21q26.2) or t(3;3)(q21;q26.2); *RPN1-EVI1*
- AML (megakaryoblastic) with t(1;22)(p13;q13); *RBM15-MKL1*
- Provisional entity: AML with mutated *NPM1*
- Provisional entity: AML with mutated *CEBPA*

Acute myeloid leukaemia with myelodysplasia-related changes

Therapy-related myeloid neoplasms

Acute myeloid leukaemia, not otherwise specified
- AML with minimal differentiation
- AML without maturation
- AML with maturation
- Acute myelomonocytic leukaemia
- Acute monoblastic/monocytic leukaemia
- Acute erythroid leukaemias
  - Pure erythroid leukaemia
  - Erythroleukaemia, erythroid/myeloid
- Acute megakaryoblastic leukaemia
- Acute basophilic leukaemia
- Acute panmyelosis with myelofibrosis

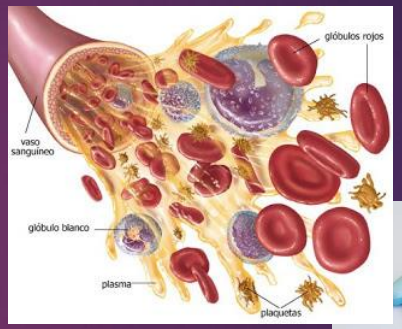
Myeloid sarcoma

Myeloid proliferations related to Down syndrome
- Transient abnormal myelopoiesis
- Myeloid leukaemia associated with Down syndrome

Blastic plasmacytoid dendritic cell neoplasms

COAGULOPATIA DE CONSUMO EN LEUCEMIAS AGUDAS

Los pacientes con neoplasias hematológicas tienen alto riesgo de complicaciones trombóticas o hemorrágicas.



- Tipo de enfermedad: Neoplasia
- Tratamiento: QMT, VVC, EPO
- Factores de riesgo general de Hospitalización

J Clin Oncol 27:4848-4857, 2009

Caso clínico presentación

Paciente de 53 años, trabajador forestal consulta por historia de 1 semana de evolución de osteomialgias, fiebre, síntomas respiratorios. Consulta en asistencia pública, se toma hemograma que informa: Hb 10 gr/dl VCM 85fl GB 34.000/mm3 promielocitos 15% mielocitos 2% juveniles 2% baciliformes 4% Neutrófilos 49% linfocitos 25% monocitos 3% plaquetas 57.000/mm3
PT 58% TTPA 45”
En que patologías piensa?

a) Sepsis reacción leucemoide
b) Leucemia aguda
c) Leucemia crónica
d) Síndrome Hanta Virus
e) Todas las anteriores

Caso clínico presentación

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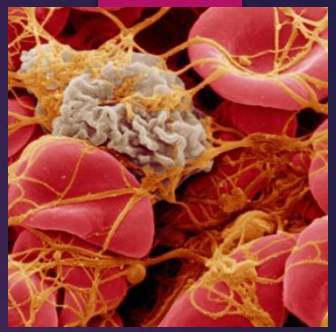
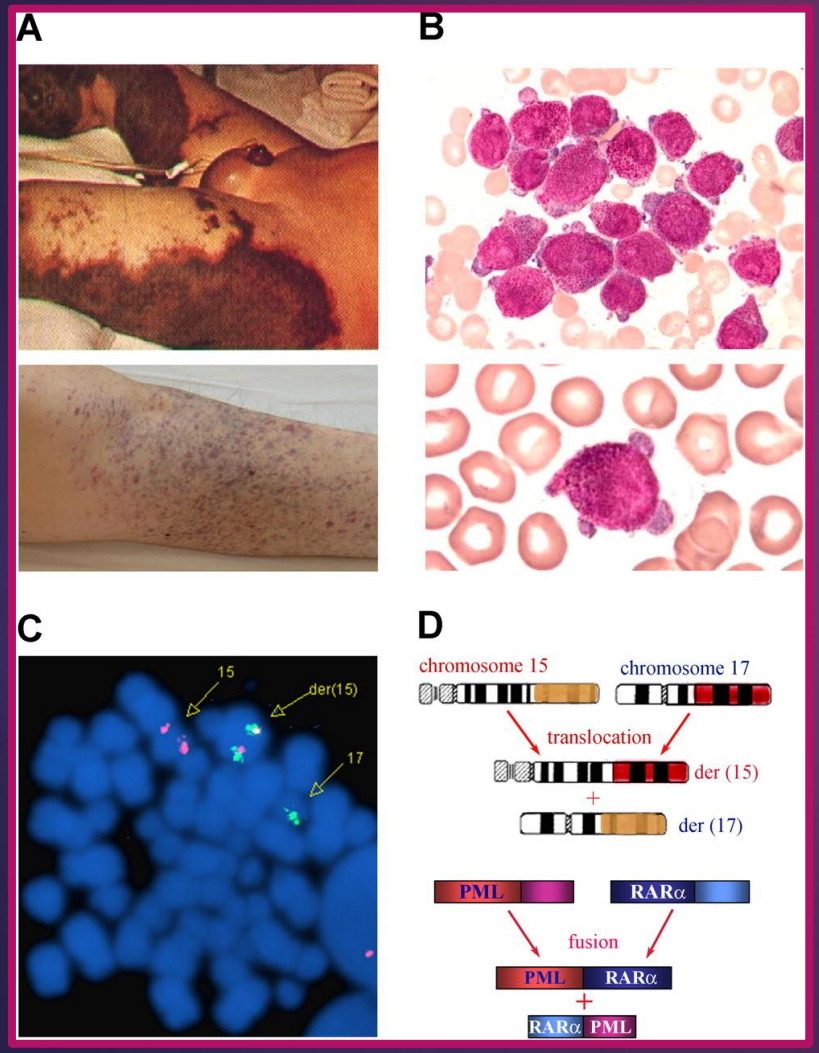
e) Todas las anteriores

- LEUCEMIA MIELOIDE AGUDA M3 PROMIELOCITICA.



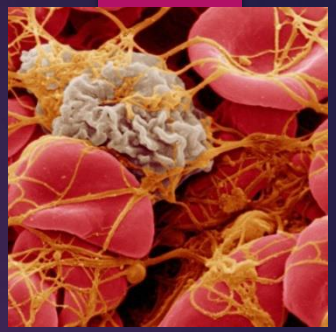


5-20% DE LAS LMA

- HEMORRAGIPARO (CID)
- ↑ DE PROMIELOCITOS
- T(15;17) (q24.1;21.2);PML-RARA

Zhen-Yi Wang, and Zhu Chen Blood 2008;111:2505-2515

- LEUCEMIA MIELOIDE AGUDA M3 PROMIELOCITICA.



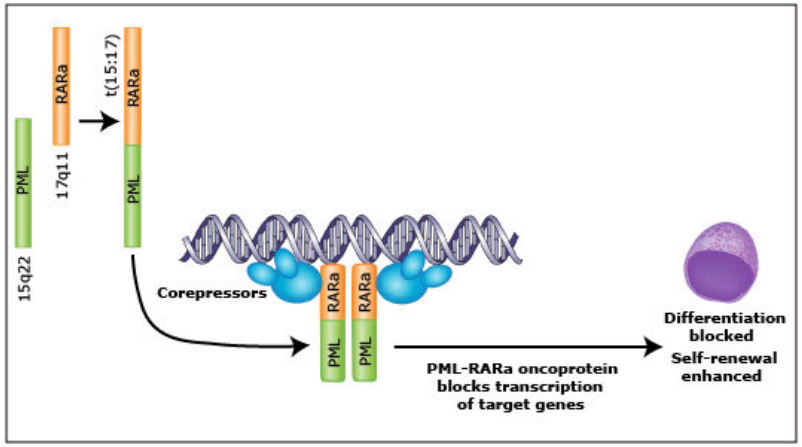
-

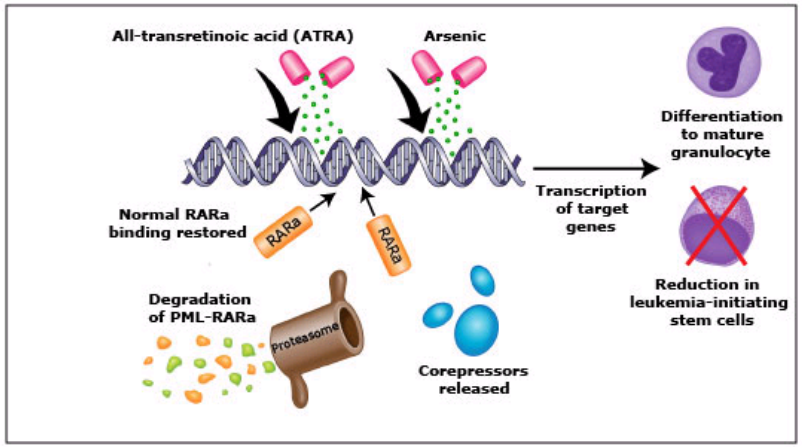
Diagnóstico diferencial

- Trastornos reactivos de la medula ósea
- Otras LMA
- Uso de factores de crecimiento
- Leucemia mieloide crónica

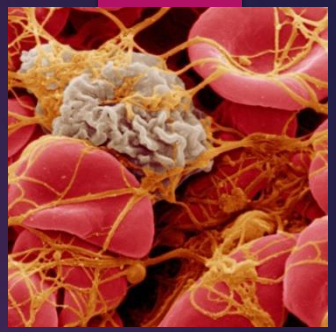
Hematología, Williams cap. 82

PML-RARa action in acute promyelocytic leukemia





Acute promyelocytic leukemia is characterized by a translocation involving the retinoic acid receptor-alpha (RARa) locus on chromosome 17. In over 90 percent of cases, there is a balanced translocation t(15;17)(q24.1;q21.1) involving the ubiquitously expressed PML gene on chromosome 15, resulting in a PML-RARa fusion protein. As shown in the upper diagram, this PML-RARa fusion protein forms a homodimer that binds to RARa target genes and acts with corepressors to block transcription of these genes. This results in blocked differentiation and enhanced self-renewal of the promyelocytes. As shown in the lower diagram, the addition of all-trans retinoic acid (ATRA) and/or arsenic trioxide results in degradation of the PML-RARa fusion protein and release of the corepressors. This allows the normal RARa to bind to target genes and promote transcription leading to differentiation of the promyelocyte to a mature granulocyte.

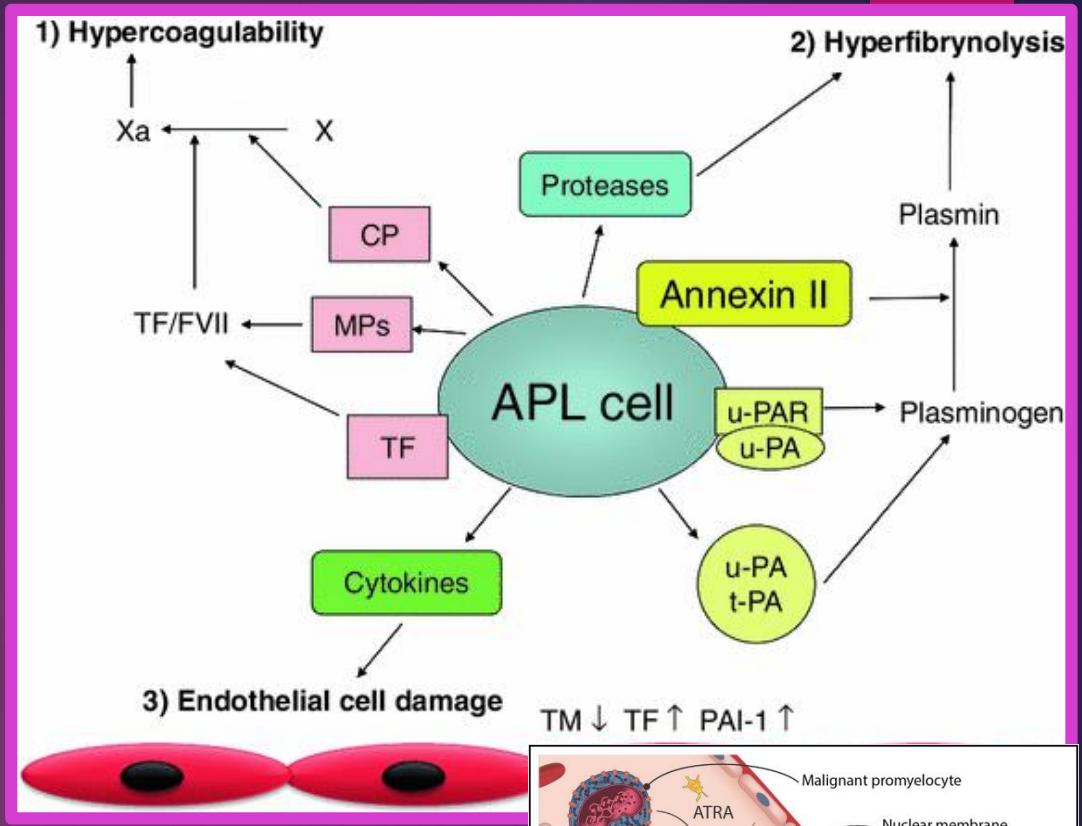


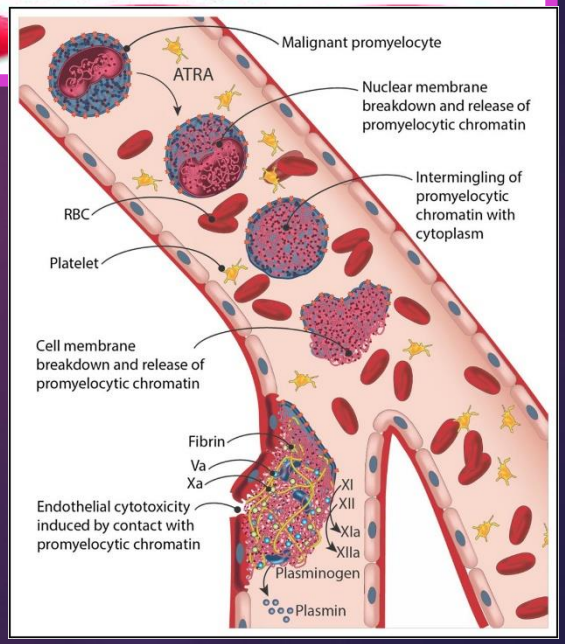
Coagulopatía LPM mecanismos

- CID
- FT ↑ expresión
- Muerte de la célula LPM: Etosis

- Hiperfibrinolisis primaria (anexina II)

- Fibrinolisis
- Proteolisis directa de
- varias proteínas





generación trombina y formación de fibrina

- Trombocitopenia
- Liberación de productos celulares (al iniciar inducción)

Thrombosis Research 125 Suppl. 2 (2010) S51–S54

Contents lists available at ScienceDirect

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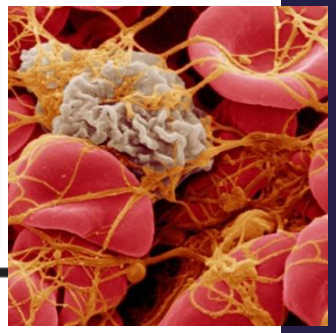


Open issues on bleeding and thrombosis in acute promyelocytic leukemia

Miguel A. Sanz*, Pau Montesinos

Hospital Universitario La Fe, Valencia, Spain

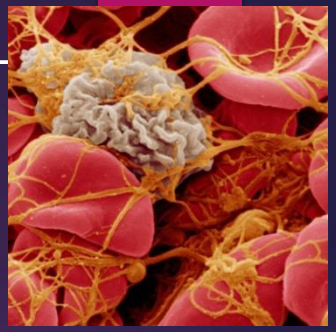
ARTICLE INFO

Keywords:
Acute promyelocytic leukemia
Bleeding
Thrombosis
Coagulopathy
Disseminated intravascular coagulation

ABSTRACT

Acute promyelocytic leukemia (APL) is a distinct subtype of acute myeloid leukemia characterized by a specific genetic alteration, affecting the retinoic acid receptor-alpha (RAR-alpha), and leading to the accumulation of the promyelocytic blasts in the bone marrow and blood which is frequently associated with a life-threatening consumptive coagulopathy. The body of biological information on APL establishes this leukemia as a unique entity that has to be promptly recognized to counteract the coagulopathy, especially in light of its striking response to treatment with all-trans retinoic acid. In fact, the current standard for induction therapy results in extremely high antileukemic efficacy, achieving 90 to 95% complete remission rate. However, while primary leukemia resistance has virtually disappeared as a cause of remission induction failure, death due to hemorrhage remains the major problem during the early treatment phase. As a part of the clotting activation commonly present in APL, thrombosis is a less recognized and probably underestimated life-threatening manifestation in patients with this disease. In addition to reviewing the available data on the incidence, outcome and prognostic factors of bleeding and thrombosis in APL, we discuss the current consensus and controversies on the most appropriate management of these complications.

LPM causas de muerte durante inducción estudio PETH

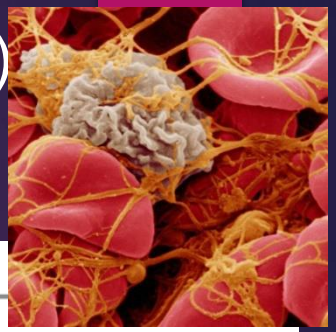


5% Hemorragia
65% HIC, 32% Pulmonar y 1 caso GI
2,3 % infección
1,4% DS

Hemorragias letales mediana día 6 para HIC (1-21)
La mayoría sobre una trombosis extensa
Hemorragia pulmonar 9 días (1-23)
La mayoría de las hemorragia letales fallecen en las primeras 24 hrs de iniciada la hemorragia

No se han establecido claramente factores predictores de hemorragia: recuento de blastos, creatininemia, signos biológicos de coagulopatía

Mortalidad precoz “ en el mundo real” (no en Trials)
17 a 20% v/s 5%



CLINICAL TRIALS AND OBSERVATIONS

Early death rate in acute promyelocytic leukemia remains high despite all-*trans* retinoic acid

Jae H. Park,[1] Baozhen Qiao,[2] Katherine S. Panageas,[3] Maria J. Schymura,[2] Joseph G. Jurcic,[1] Todd L. Rosenblat,[1] Jessica K. Altman,[4] Dan Douer,[1] Jacob M. Rowe,[5] and Martin S. Tallman[1]

[1]Leukemia Service, Memorial Sloan-Kettering Cancer Center, New York, NY; [2]New York State Cancer Registry, NY State Department of Health, Albany, NY; [3]Department of Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, NY; [4]Northwestern University, Feinberg School of Medicine, Chicago, IL; and [5]Rambam Medical Center, Technion, Haifa, Israel

The incidence of early death in a large population of unselected patients with acute promyelocytic leukemia (APL) remains unknown because of the paucity of outcome data available for patients treated outside of clinical trials. We undertook an epidemiologic study to estimate the true rate of early death with data from the Surveillance, Epidemiology, and End Results (SEER) program. A total of 1400 patients with a diagnosis of APL between 1992 and 2007 were identified. The overall early death rate was 17.3%, and only a modest change in early death rate was observed over time. The early death rate was significantly higher in patients aged ≥ 55 years (24.2%; $P < .0001$). The 3-year survival improved from 54.6% to 70.1% over the study period but was significantly lower in patients aged ≥ 55 years (46.4%; $P < .0001$). This study shows that the early death rate remains high despite the wide availability of all-*trans* retinoic acid and appears significantly higher than commonly reported in multicenter clinical trials. These data highlight a need to educate health care providers across a wide range of medical fields, who may be the first to evaluate patients with APL, to have a major effect on early death and the cure rate of APL. (*Blood.* 2011;118(5): 1248-1254)

Jae H Blood 2011 118 5 1248

Incidence and Risk Factors for Thrombosis in Patients with Acute Promyelocytic Leukemia. Experience of the PETHEMA LPA96 and LPA99 Protocols.

Pau Montesinos, Javier de la Serna, Edo Vellenga, Consuelo Rayon, Juan Bergua, Ricardo Parody, Jordi Esteve, Marcos Gonzalez, Salud Brunet and Miguel Sanz

Blood 2006 108:1503;

Acido tranexámico no muestra beneficio es cuestionable
su uso no disminuye hemorragia y hay tendencia a aumentar trombosis

Results: 39/759 patients (5.1%) developed thrombosis. Among 26 patients who died before initiation of CT, 6 (23%) presented with thrombotic complications: 3 cerebral stroke (CNS), 2 pulmonary embolism (PE) and 1 acute myocardial infarction (AMI). Thirty-three (4.5%) of the 733 patients in whom CT was initiated experienced thrombosis: 3 at diagnosis (1 AMI, 1 CNS and 1 deep venous thrombosis (DVT)) and 30 after the start of CT (16 DVT, 6 CNS, 3 PE, 2 AMI and 2 others). Four thrombotic events were related with initiation of tranexamic acid: 2 DVT, 1 skin necrosis and 1 renal necrosis. The following factors were related to a higher incidence of thrombosis: leukocytes $>10\times10^9$/L (9% vs 4%, p<0.01), M3-variant subtype (11 4%, p=0.02), fibrinogen <170 mg/dl (7% vs 3%, p=0.02) and hemoglobin >10 g (8% vs 4%, p=0.03). No significant relation was observed with CD2 or other surf antigens, as well as FLT3 mutations. Use of tranexamic acid showed a trend tow a higher incidence of thrombosis (6% vs 3%, p=0.08). In multivariate analysis hypofibrinogenemia and M3-v subtype remained as independent prognostic fac Thrombosis was related with a higher induction mortality (including deaths befc start of CT), 28% vs 11%, p<0.01.

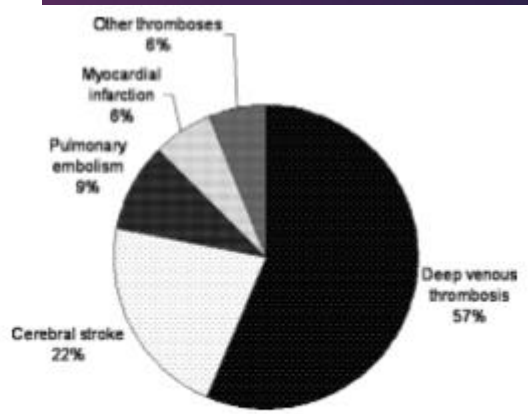
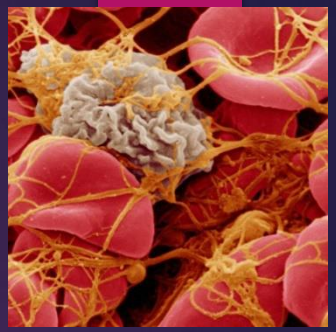


Fig. 2. Type of thrombotic events during induction therapy with AIDA regimen in APL patients.

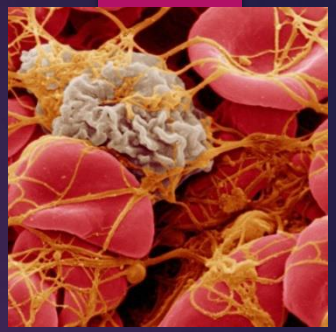
LABORATORIO



Control de la coagulopatía

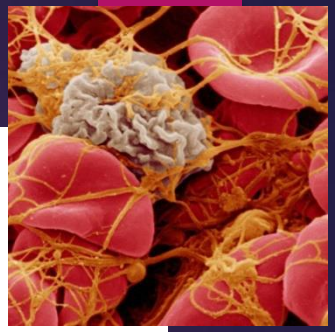
- Monitorización estrecha de parámetros:
- Fibrinógeno.
- Dímero D
- PT
- TTPA
- Recuento plaquetas

Manifestaciones clínicas Coagulopatía de consumo al diagnostico LPM en un 80% de los casos



- Hipofibrinogenemia
- trombocitopenia
- TTPa TP elevados
- D dímero elevados

- Hemorragia mucocutánea: petequias, equimosis
- HIC
- Hemorragia pulmonar
- Trombosis



Leukemia (2011) 25, 1128–1134

www.nature.com/leu

ORIGINAL ARTICLE

Continuing high early death rate in acute promyelocytic leukemia: a population-based report from the Swedish Adult Acute Leukemia Registry

S Lehmann[1,9], A Ravn[1], L Carlsson[1], P Antunovic[2,9], S Deneberg[1], L Möllgård[1,9], Å Rangert Derolf[3,9], D Stockelberg[4,9], U Tidefelt[5,9], A Wahlin[6,9], L Wennström[4,9], M Höglund[7,9] and G Juliusson[8,9]

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Our knowledge about acute promyelocytic leukemia (APL) patients is mainly based on data from clinical trials, whereas population-based information is scarce. We studied APL patients diagnosed between 1997 and 2006 in the population-based Swedish Adult Acute Leukemia Registry. Of a total of 3897 acute leukemia cases, 3205 (82%) had non-APL acute myeloid leukemia (AML) and 105 (2.7%) had APL. The incidence of APL was 0.145 per 100 000 inhabitants per year. The median age at the time of diagnosis was 54 years; 62% were female and 38% male. Among younger APL patients, female sex predominated (89% of patients <40 years). Of the 105 APL patients, 30 (29%) died within 30 days (that is, early death (ED)) (median 4 days) and 28 (26%) within 14 days from diagnosis. In all, 41% of the EDs were due to hemorrhage; 35% of ED patients never received all-*trans*-retinoic acid treatment. ED rates increased with age but more clearly with poor performance status. ED was also associated with high white blood cells, lactate dehydrogenase, creatinine, C-reactive protein and low platelet count. Of non-ED patients, 97% achieved complete remission of which 16% subsequently relapsed. In total, 62% are still alive at 6.4 years median follow-up. We conclude that ED rates remain very high in an unselected APL population.
Leukemia (2011) 25, 1128–1134; doi:10.1038/leu.2011.78;
published online 19 April 2011

or other comorbidities.[1,3–5] Sanz *et al.*[6] report that half of the patients excluded from the Spanish PETHEMA trials (LPA 96 and LPA 99) were excluded due to life-threatening hemorrhages. Patients may also die before any treatment has been initiated and even before diagnosis.[7] Thus, unselected APL populations probably have higher early death (ED) rates compared with clinical trials.

Despite the improvements in APL treatment, ED remains a problem with reported ED rates ranging between 7 and 14%.[3–5,8–10] Recently, Jacomo *et al.* reported an ED rate of 32% in a study of APL patients at 12 Brazilian institutions receiving treatment with ATRA and anthracyclines. Hemorrhages, caused by disseminated intravascular coagulation, hypercoagulability, fibrinolysis, proteolysis and thrombocytopenia, constitute the major cause of death with the central nervous system (CNS) being the most common site of bleeding.[11,12] Other causes of ED in APL are infections, multiorgan failure and the differentiation syndrome.[13,14]

In order to assess 'real world' data on ED as well as on other aspects of an unselected APL population, we analyzed patients diagnosed with APL and reported to the Swedish Acute

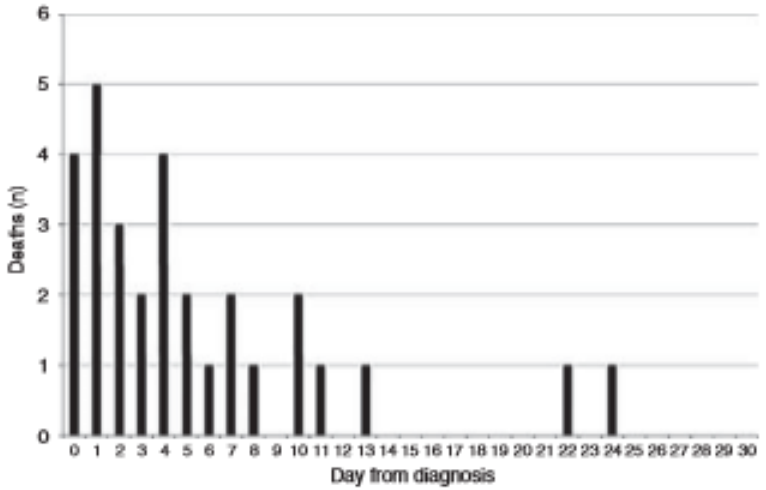


Figure 1 Number of patients with EDs according to days from diagnosis to death.

Table 2 Early mortality rates (30 days) in APL and non-APL AML by age and WHO performance status

	APL			*AML (non-APL)*		
	ED	*Total*	*ED (%)*	*ED*	*Total*	*ED (%)*
16–29 years	3	16	18.8	2	76	2.6
30–39 years	1	12	8.3	4	117	3.4
40–49 years	3	21	14.3	11	201	5.5
50–59 years	3	16	18.8	46	406	11.4
60–69 years	10	17	58.8	82	644	12.8
70–79 years	7	18	38.9	203	999	20.3
80+ years	3	5	60.0	261	770	33.9
WHO 0	2	28	7.1	29	492	5.9
WHO I	3	28	11	93	1232	7.5
WHO II	6	20	30	140	703	20
WHO III –and IV	18	23	78	324	685	47

Abbreviations: AML, acute myeloid leukemia; APL, acute promyelocytic leukemia; ED, early death; WHO, World Health Organization.

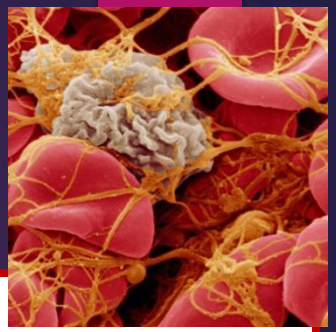


Table 3 Causes of death

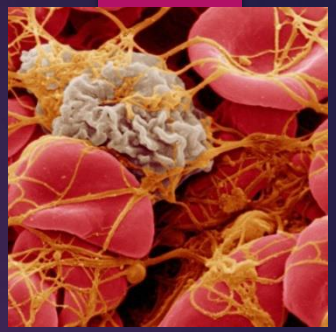
Cause of death	*ED patients (%)*
Bleeding total	12 (41)
CNS bleeding	11 (38)
Pulmonary bleeding	1 (3.4)
Cardiac or respiratory failure	5 (17)
Sepsis	3 (10)
Multiorgan failure	2 (6.9)
Suspected DS	1 (3.4)
Cerebral infarction	1 (3.4)
Cerebral leukostasis	1 (3.4)
Unknown	3 (10)

Abbreviations: CNS, central nervous system; DS, differentiation syndrome; ED, early death.

Treatment advances have not improved the early death rate in acute promyelocytic leukemia

James Scott McClellan,[1,2*] Holbrook E. Kohrt[1*] Steven Coutre,[1] Jason R. Gotlib,[1] Ravindra Majeti,[1,2] Ash A. Alizadeh,[1,2#] and Bruno C. Medeiros[1#]

[1]Department of Medicine, Division of Hematology, Stanford University School of Medicine, Stanford, CA; and [2]Stanford Institute for Stem Cell Biology and Regenerative Medicine, Palo Alto, CA, USA



ABSTRACT

Early mortality in acute promyelocytic leukemia has been reported to occur in less than 10% of patients treated in clinical trials. This study reports the incidence and clinical features of acute promyelocytic leukemia patients treated at Stanford Hospital, CA, USA since March 1997, focusing on early mortality. We show that the risk of early death in acute promyelocytic leukemia patients is higher than previously reported. In a cohort of 70 patients who received induction therapy at Stanford Hospital, 19% and 26% died within seven and 30 days of admission, respectively. High early mortality was not limited to our institution as evaluation of the Surveillance, Epidemiology and End Results Database demonstrated that 30-day mortality for acute promyelocytic leukemia averaged 20% from 1977-2007 and did not improve significantly over this interval. Our findings show that early death is now the greatest contributor to treatment failure in this otherwise highly curable form of leukemia.

Key words: acute promyelocytic leukemia, early death, treatment, incidence, predictors.

Citation: McClellan JS, Kohrt HE, Coutre S, Gotlib JR, Majeti

Incidence and predictors of early death in APL

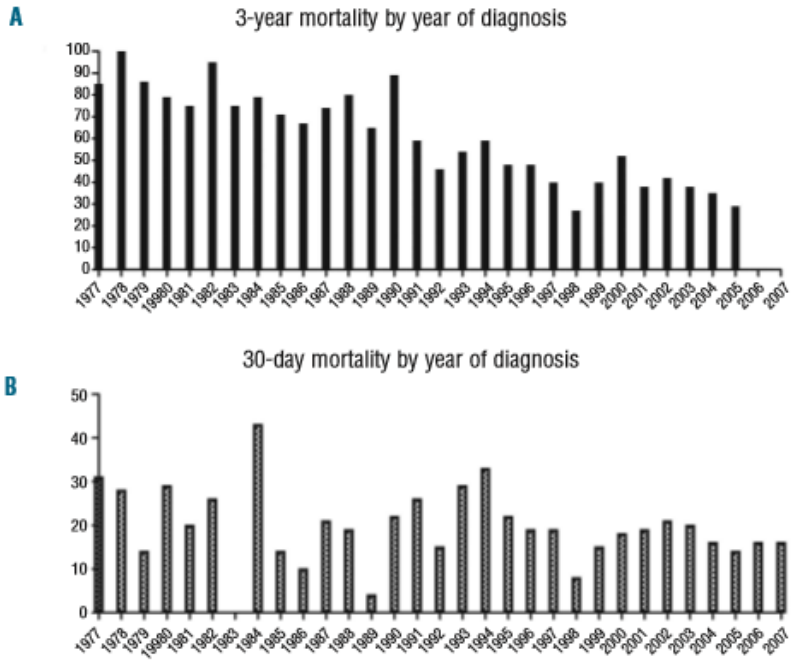
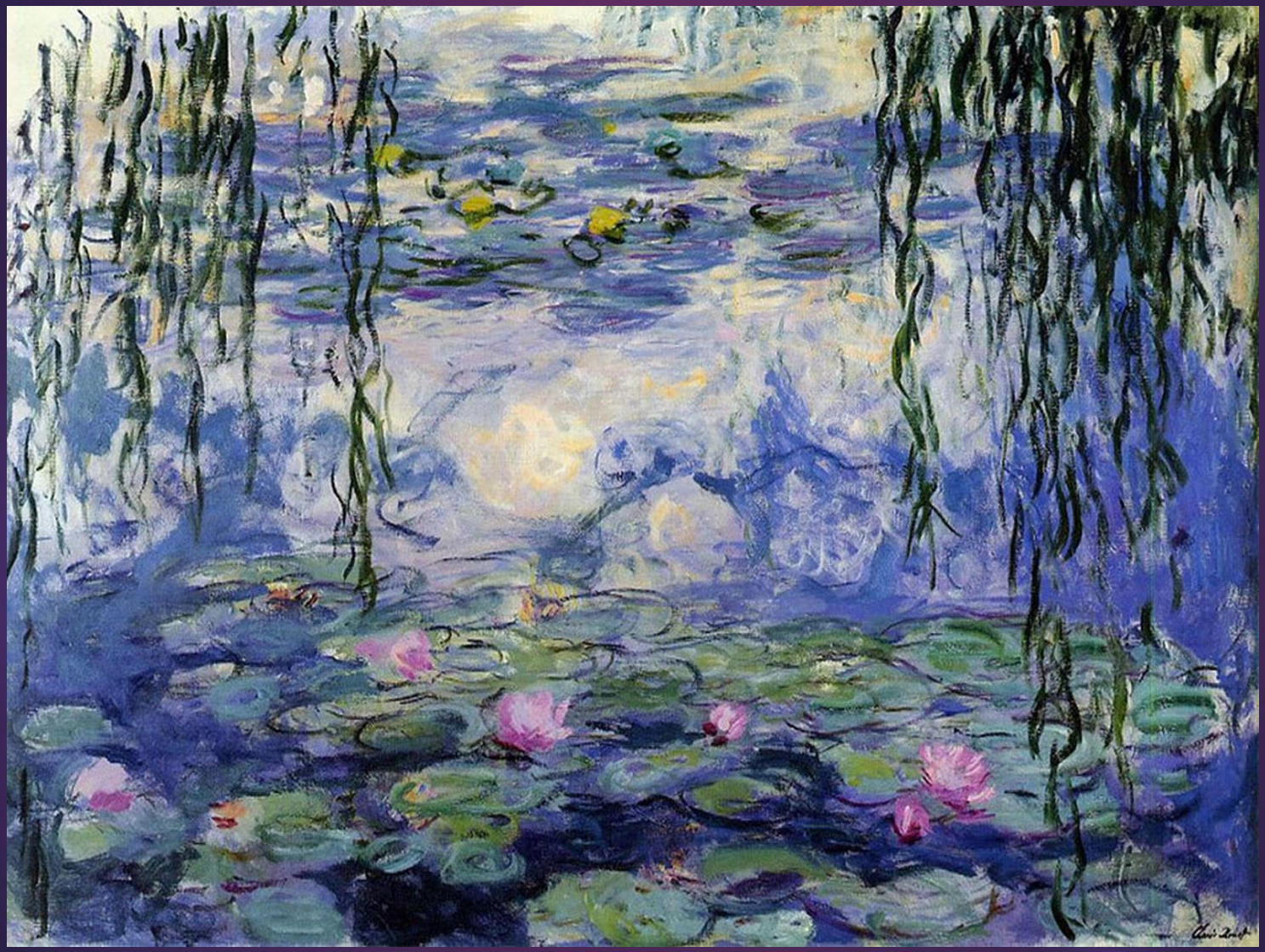


Figure 2. (A) Three-year and (B) 30-day mortality of APL patients in the SEER databse, 1977-2007.



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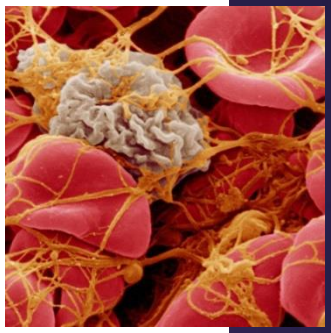
doi:10.1093/annonc/mdw171
Published online 15 April 2016

Current management of newly diagnosed acute promyelocytic leukemia



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The management of acute promyelocytic leukemia (APL) has considerably evolved during the past two decades. The advent of all-*trans* retinoic acid (ATRA) and its inclusion in combinatorial regimens with anthracycline chemotherapy has provided cure rates exceeding 80%; however, this widely adopted approach also conveys significant toxicity including severe myelosuppression and rare occurrence of secondary leukemias. More recently, the advent of arsenic trioxide (ATO) and its use in association with ATRA with or without chemotherapy has further improved patient outcome by allowing to minimize the intensity of chemotherapy, thus reducing serious toxicity while maintaining high anti-leukemic efficacy. The advantage of ATRA–ATO over ATRA chemotherapy has been recently demonstrated in two large randomized trials

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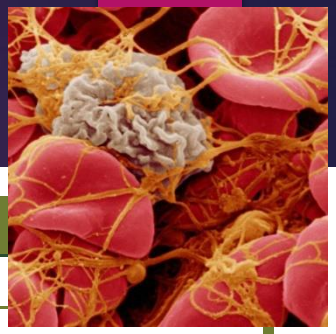
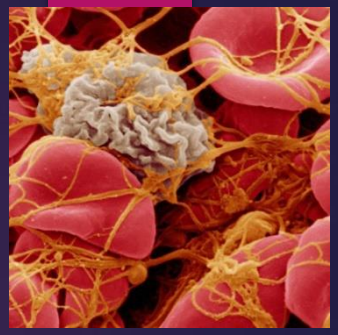


Table 1. Recommendations for initial management of APL

Management measures	Recommendations	Open issues
Transfusional supportive care	Intensive transfusion support with plasma and platelet concentrates to maintain platelets 30–50 × 10^9/l and fibrinogen >1.5 g/l. Strict monitoring of blood count and coagulation profile (every 6 h in high-risk patients)	Benefit of antifibrinolytic, anticoagulant (heparins) and procoagulant (e.g. recombinant activated Factor VII) agents is controversial
Initiation of therapy with ATRA and/or ATO	Upon morphologic or clinical suspect of APL, therapy with ATRA and/or ATO should be started without waiting for genetic confirmation of diagnosis	
Genetic diagnosis	Diagnostic confirmation at genetic level is mandatory. FISH and/or RT-PCR are preferred tests to rapidly identify PML-RARA.	
Lumbar puncture, placement of CVC line, leukapheresis and other invasive procedures	To be avoided in light of the augmented risk of bleeding and/or thrombosis	
Prophylaxis of differentiation syndrome	Prophylaxis with steroids is commonly recommended, particularly in patients with elevated WBC (>5 × 10^9/l).	Type of steroid (methylprednisolone or dexamethasone) and duration of prophylaxis

Tratamientos de la coagulopatía PANDA

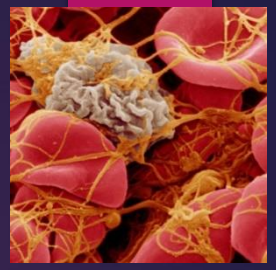


- Hemograma, PT, TTPK y fibrinógeno cada 12 ó 24 horas desde el ingreso hasta resolución de la coagulopatía.

- Plaquetas < 30.000/l transfundir 1 Unidad de plaquetas por cada 10 Kg de peso EV.
- PT < 60% y/o TTPK > 1,5 valor normal, transfundir plasma fresco congelado, 15-20 cc/kg EV.

- Fibrinógeno <100 (o <150 con hemorragia de riesgo vital), transfundir 1 U de crioprecipitado por cada 10 kg peso EV.

- Bomba de infusión de Espercil 100 mg/kg/hr EV, ***sólo en caso de hemorragia con riesgo vital.***



Tratamientos de la coagulopatía PANDA

Para los pacientes con alto riesgo de hemorragia de riesgo vital (edad> 70 años; leucocitos> 10.000 x mm3, o creatinina > 1,4 mg / dl) la transfusión de plaquetas se debe indicar para alcanzar recuentos > a 50.000 x mm3.

El uso de heparina y antifibrinolíticos (ε-aminocaproico y el ácido analógica, tranexámico) no deben ser utilizados de regla.

Resolución de coagulopatía:

Se considera resuelta la CID cuando los exámenes de coagulación PT, TTPK, y fibrinógeno se encuentren en rangos superiores a los antes mencionados por al menos 3 días consecutivos sin apoyo transfusional.

Caso clínico presentación

Paciente de 25 años, Peso 60 kg, 10 días de evolución equimosis , hematemesis,
Asociado a cefalea sin focalidad. Hemograma Hb 8,4 gr/dl VCM 86fl GB 36600/mm3 Blastos 66% Neutrófilos 12% linfocitos 8% monocitos 3% plaquetas 18.000/mm3
Bastones de Auer. PT 48% TTPA 50” Fibrinógeno 80

Indicaría transfusión de:

a) Plaquetas 6 U, GR 2 U, Criopp 12 U, PFC 600 cc
b) Plaquetas 12 U, GR 1 U, Criopp 3 U, PFC 200cc
c) Plaquetas 6 U, Criopp 6 U, PFC 900cc
d) GR 2 U, Criopp 6 U, PFC 900 U
e) Plaquetas 6 U, GR 2 U, PFC 900 cc

Caso clínico presentación

Paciente de 25 años, Peso 60 kg, 10 días de evolución equimosis , hematemesis,
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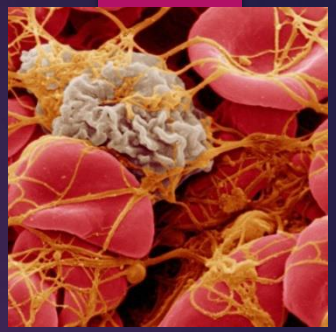
c) Plaquetas 6 U, Criopp 6 U, PFC 900cc
d) GR 2 U, Criopp 6 U, PFC 900 U
e) Plaquetas 6 U, GR 2 U, PFC 900 cc

Table 1. Suggested guidelines for supportive care measures and initial approach to patients with APL

Guideline	Summary
1	Institute ATRA without delay at first suspicion of the diagnosis without waiting for cytogenetic or molecular genetic confirmation.
2	Check CBC and DIC screens 3 or 4 times a day to maintain platelet count more than 30 000 to 50,000/μL and fibrinogen more than 150 mg/dL with transfusions of platelets and cryoprecipitate several times a day to maintain these levels.
3	Avoid leukapheresis.
4	Avoid routine lumbar puncture.
5	Avoid placement of central venous catheter.
6	Be vigilant in diagnosing APL differentiation syndrome; if present, administer dexamethasone 10 mg/m^2 per day until complete resolution of the signs and symptoms. Resume ATRA or ATO (if it had been stopped) under the coverage of corticosteroids.
7	Avoid myeloid growth factors in induction.
8	Give dexamethasone for high-risk patients with leukocytosis with WBC more than or equal to 30 000-50 000/μL.
9	Do not obtain a bone marrow aspirate and biopsy at the nadir during induction.

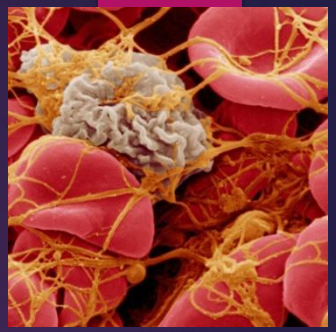


The NEW ENGLAND JOURNAL of MEDICINE

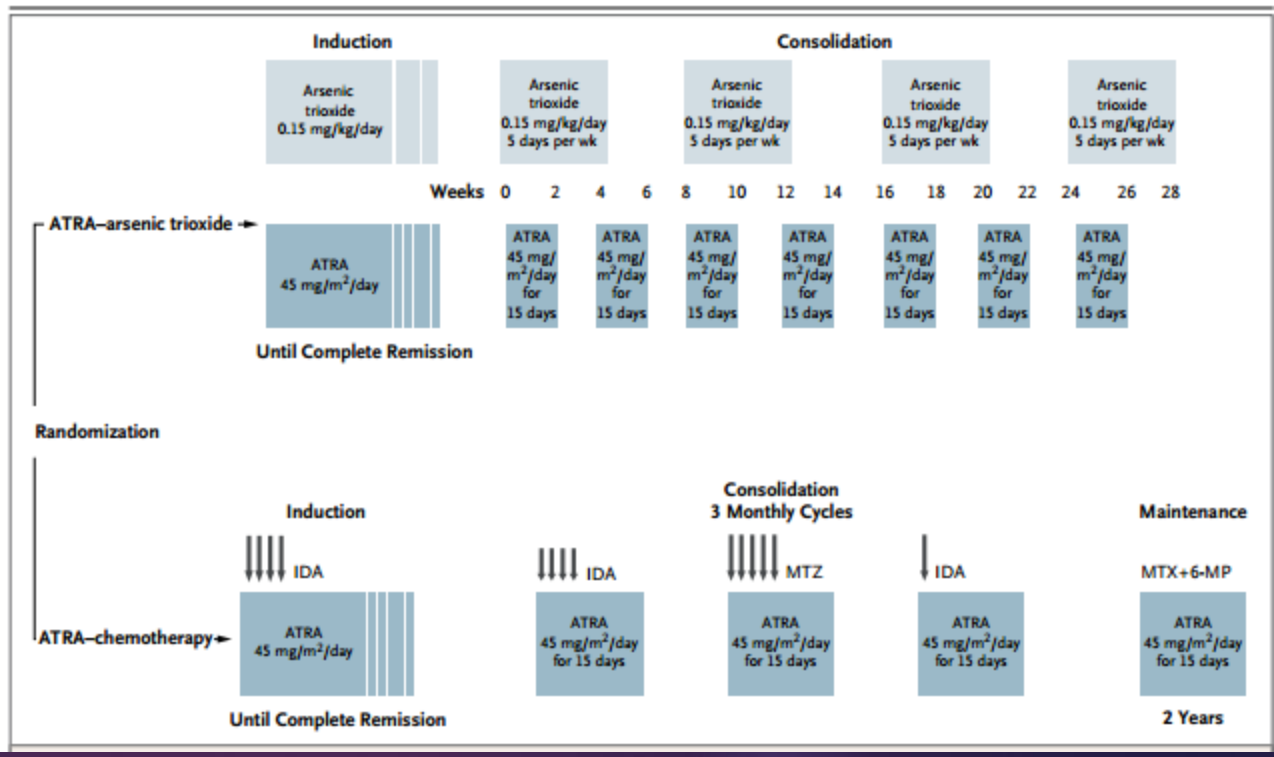
ESTABLISHED IN 1812 JULY 11, 2013 VOL. 369 NO. 2

Retinoic Acid and Arsenic Trioxide for Acute Promyelocytic Leukemia

F. Lo-Coco, G. Avvisati, M. Vignetti, C. Thiede, S.M



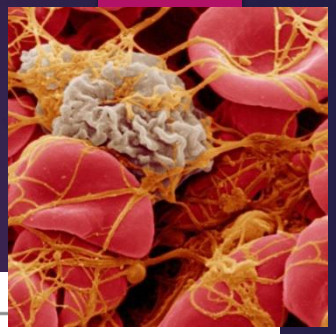
RETINOIC ACID AND ARSENIC TRIOXIDE FOR APL



FUTURO….

Disminuir la tasa de mortalidad precoz
20-30% v/s 3-5%

1992-1995 22,1 %
1996-2001 14,7
2002-2007 17,5



CLINICAL TRIALS AND OBSERVATIONS

Early death rate in acute promyelocytic leukemia remains high despite all-*trans* retinoic acid

Jae H. Park,[1] Baozhen Qiao,[2] Katherine S. Panageas,[3] Maria J. Schymura,[2] Joseph G. Jurcic,[1] Todd L. Rosenblat,[1] Jessica K. Altman,[4] Dan Douer,[1] Jacob M. Rowe,[5] and Martin S. Tallman[1]

[1]Leukemia Service, Memorial Sloan-Kettering Cancer Center, New York, NY; [2]New York State Cancer Registry, NY State Department of Health, Albany, NY; [3]Department of Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, NY; [4]Northwestern University, Feinberg School of Medicine, Chicago, IL; and [5]Rambam Medical Center, Technion, Haifa, Israel

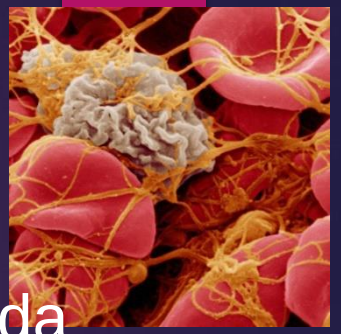
The incidence of early death in a large population of unselected patients with acute promyelocytic leukemia (APL) remains unknown because of the paucity of outcome data available for patients treated outside of clinical trials. We undertook an epidemiologic study to estimate the true rate of early death with data from the Surveillance, Epidemiology, and End Results (SEER) program. A total of 1400 patients with a diagnosis of APL between 1992 and 2007 were identified. The overall early death rate was 17.3%, and only a modest change in early death rate was observed over time. The early death rate was significantly higher in patients aged ≥ 55 years (24.2%; $P < .0001$). The 3-year survival improved from 54.6% to 70.1% over the study period but was significantly lower in patients aged ≥ 55 years (46.4%; $P < .0001$). This study shows that the early death rate remains high despite the wide availability of all-*trans* retinoic acid and appears significantly higher than commonly reported in multicenter clinical trials. These data highlight a need to educate health care providers across a wide range of medical fields, who may be the first to evaluate patients with APL, to have a major effect on early death and the cure rate of APL. (*Blood*. 2011;118(5): 1248-1254)

Introduction

Recomendación es alto nivel de sospecha inicio precoz de ATRA + terapia de soporte con Transfusiones.

Blood Cáncer Journal (2015) 304

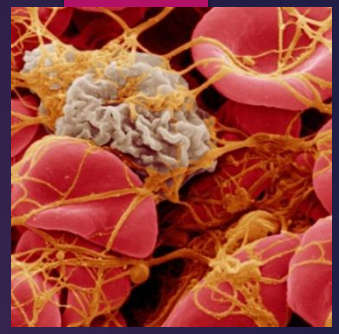
Coagulopatía de consumo en Leucemia aguda



La siguiente imagen corresponde a una pintura titulada La vida y la muerte pertenece al pintor

a) Paul Klee
b) Joan Miró
c) Marc Chagall
d) Gustav Klimt
e) Pablo Picasso

Coagulopatía en Leucemia aguda



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