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BILL MURRAY SCARLETT JOHANSSON

Lost In Translation

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The new film written and directed by Sofia Coppola

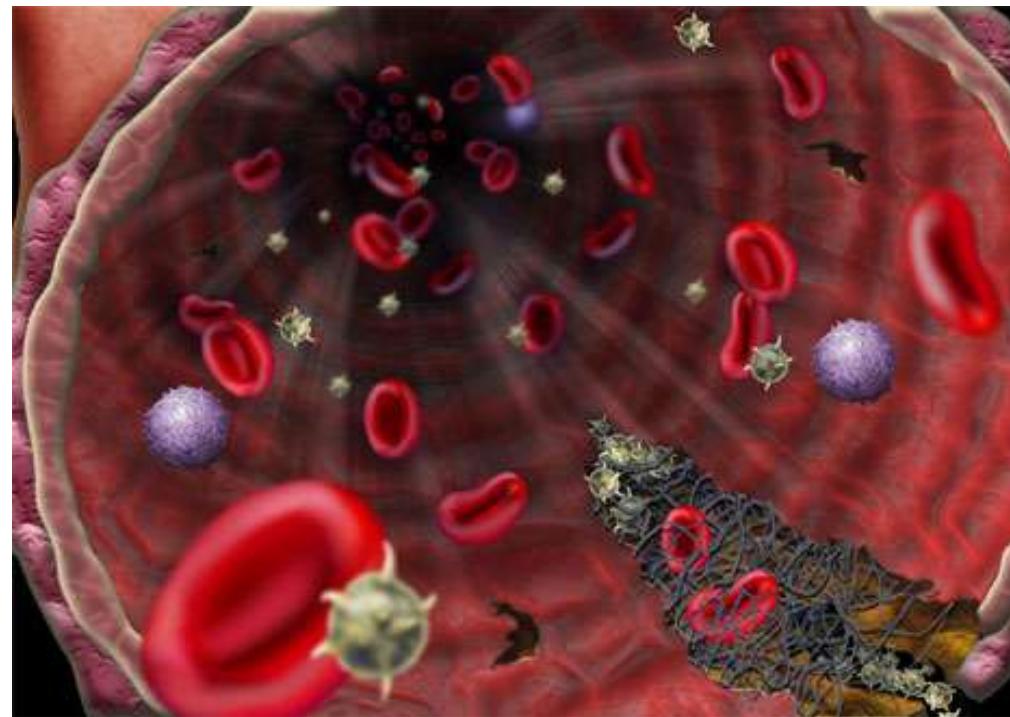
LABORATORIJSKA DIJAGNOSTIKA TROMBOFILIIA

Pristup venskom tromboembolizmu

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Koagulacija, Inst Mol Med, Karolinska Institut
Klin hemija, Karolinska Univer Lab, Karolinska Univer Boln
Stokholm, Švedska

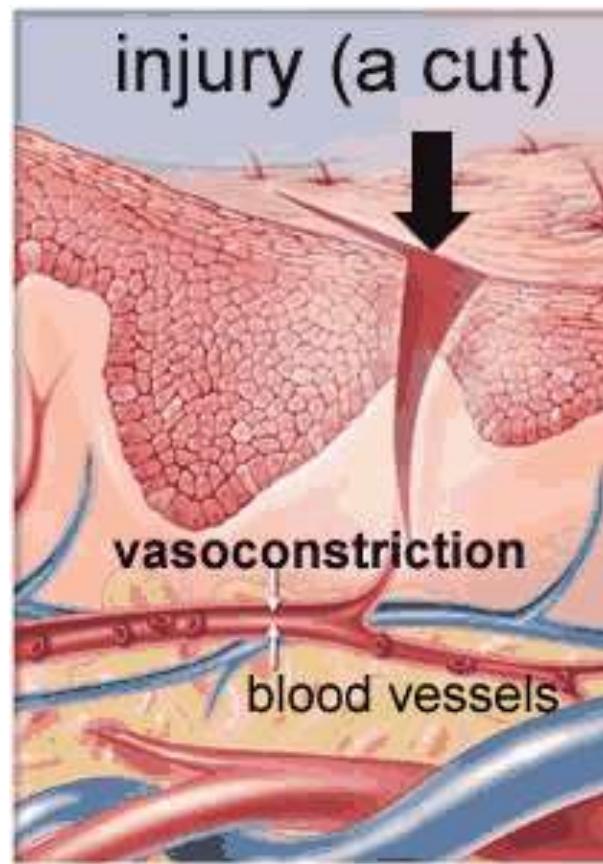


Normalna hemostaza omogućava normalan tok krvi u očuvanim krvnim sudovima

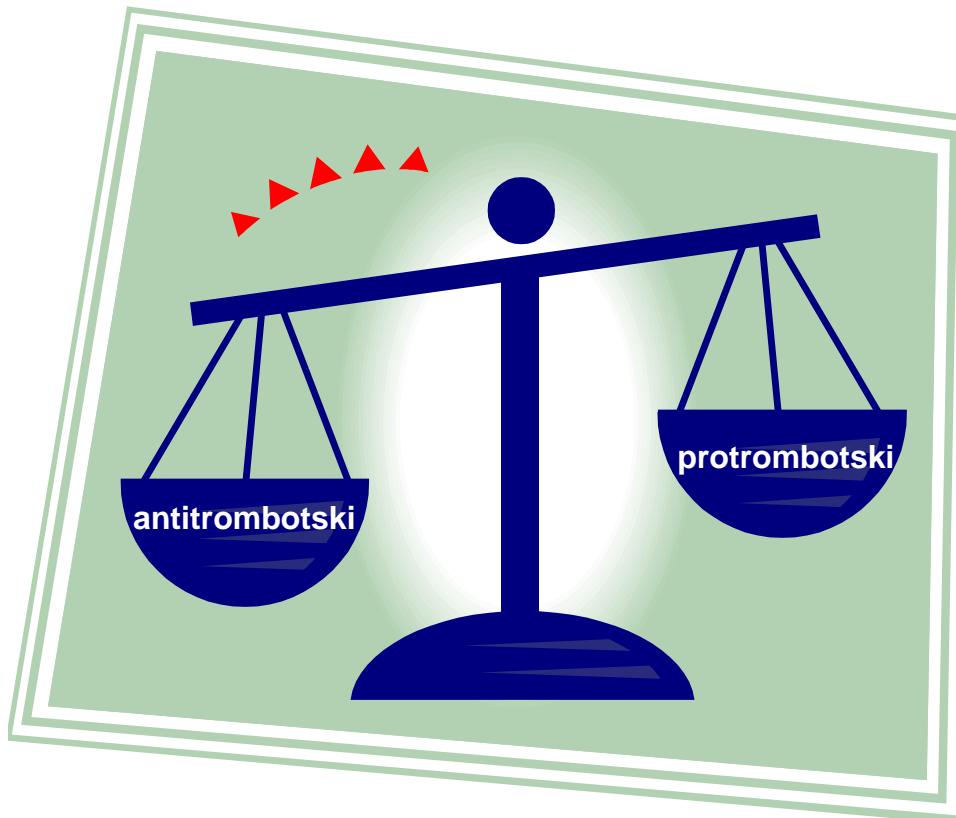


<http://www.youtube.com/watch?v=CuHhmSbxNIs>

Normalna hemostaza sprečava i zaustavlja krvarenje nakon ostećenja krvnog suda

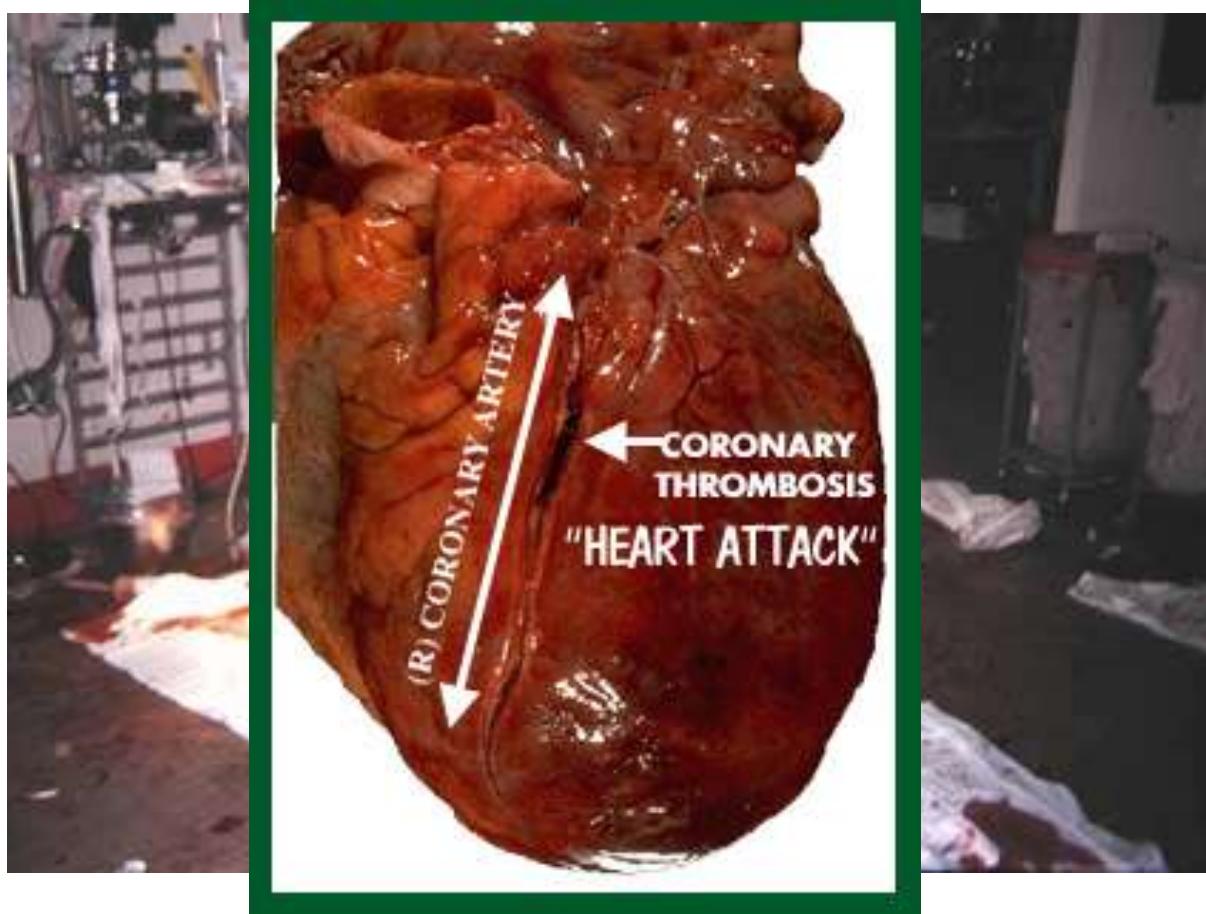


Prevencija tromboze i zaustavljanje krvarenja su posledica dejstva antitrombotskih i protrombotskih mehanizama hemostaze

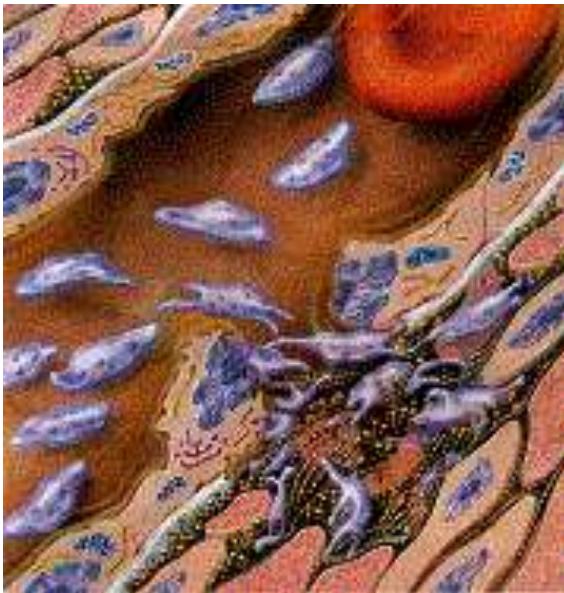
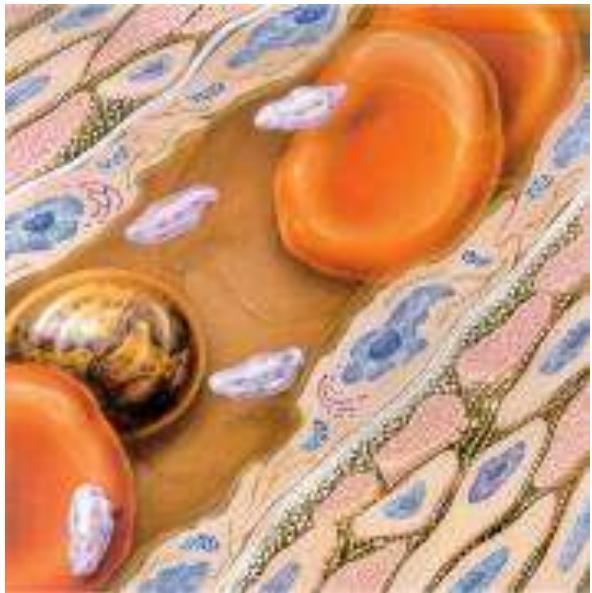


Ravnoteža između ovih mehanizama omogućava održavanje normalne homeostaze u ljudskom organizmu

Predominacija jednog od ovih mehanizama može uzrokovati hemoragijske ili trombotične poremećaje



Fiziologija normalne hemostaze



Fiziologija normalne hemostaze

Normalnu hemostazu čine četiri osnovna činioca:

- krvni sudovi
- trombociti
- koagulacija
- fibrinoliza

Poremećaj u jednom ili više od ovih činilaca može dovesti do krvarenja ili tromboza

Fiziologija normalne hemostaze

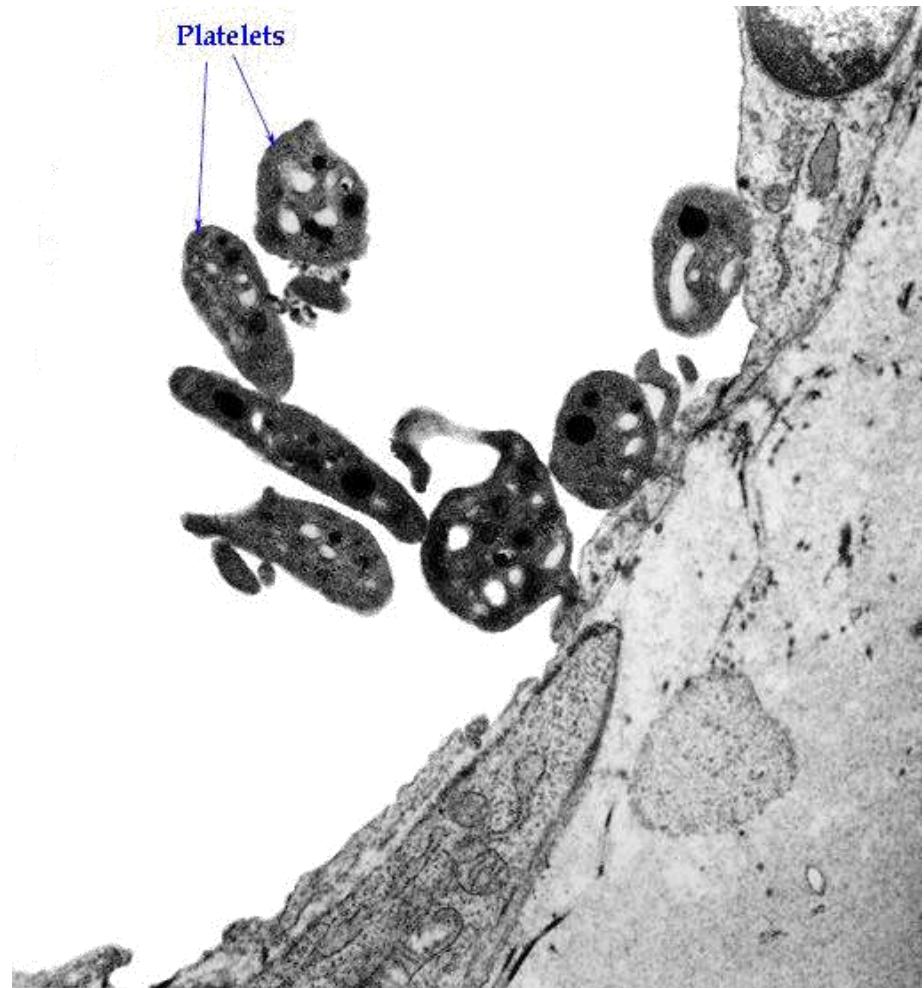
VASKULARNA:

vazokonstrikcija,
oslobađanje tkivnog
faktora (TF) i
prostaciklina



Fiziologija normalne hemostaze

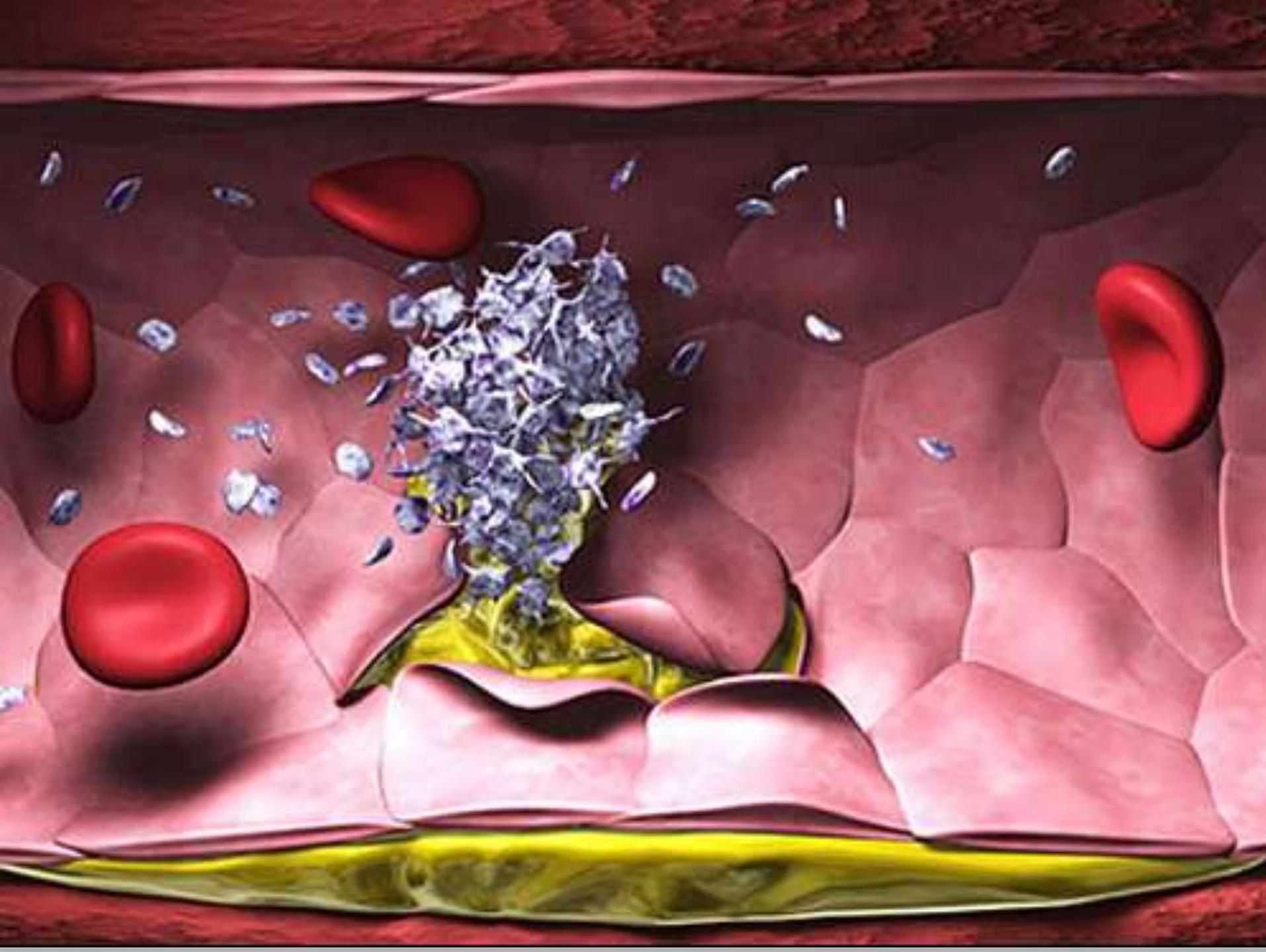
TROMBOCITI:
adhezija, oslobođanje ADP i
prostaciklina



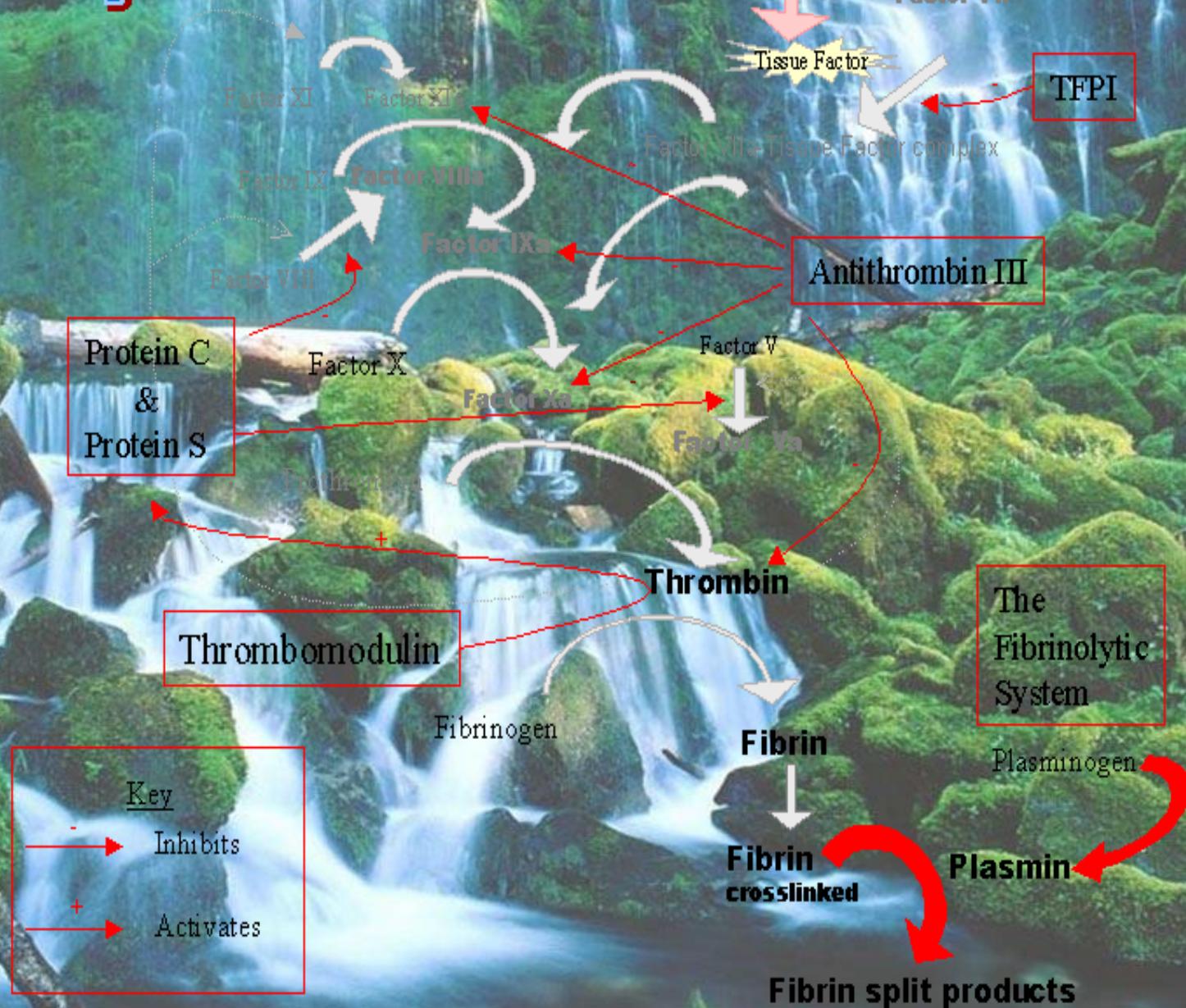
Fiziologija normalne hemostaze

TROMBOCITI:
agregacija



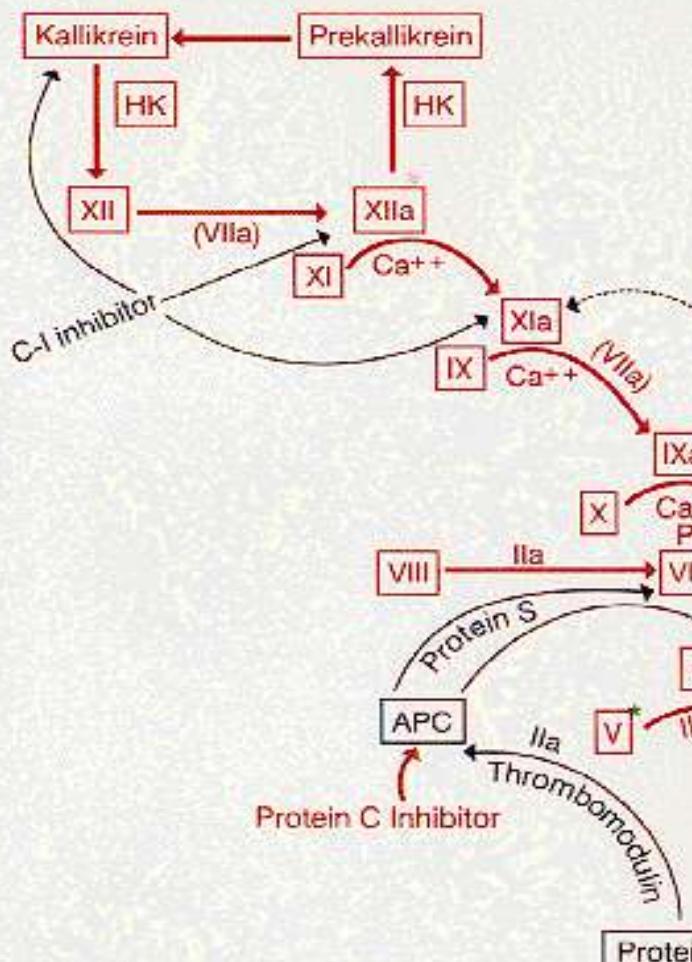


Regulation of the Cascade



Contact Factor Pathway

(Intrinsic Pathway)



Tissue Factor Pathway

(Extrinsic Pathway)

"Tissue Damage"

Tissue Factor

TFPI → Xa

VIIa ← VII

Xa ← IXa

VIIIa ← VIII

Xa ← IIa

Va ← V

IIa ← Fibrinogen

IIa ← XIIIa

Ca⁺⁺ → Fibrin Polymer

Ca⁺⁺ → Fibrin Clot

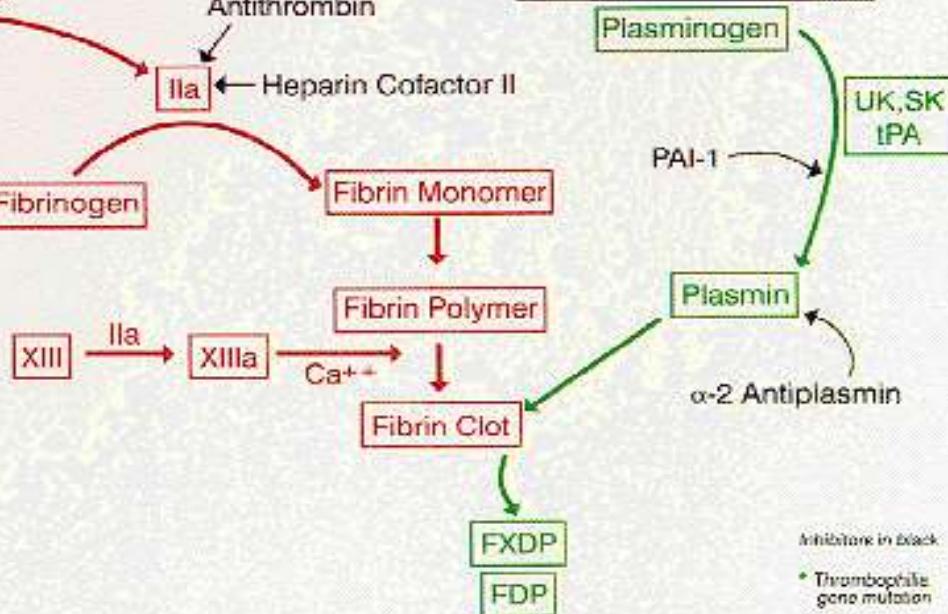
Enzyme Research Laboratories

412 S. Lafayette Blvd.
South Bend, IN U.S.A. 46601
Phone: (219) 288-2268 • Fax: (219) 288-2272
800-729-5270
E-mail Address: Info@enzymeresearch.com
Web Site: www.enzymeresearch.com

Protein Concentrations

| Component | Molecular Weight | Plasma Concentration µg/ml | Plasma Concentration µM |
|-----------------------------------|------------------|----------------------------|-------------------------|
| Fibrinogen (I) | 330,000 | 3000 | 9.09 |
| Prothrombin (II) | 72,000 | 100 | 1.385 |
| Factor V | 330,000 | 10 | 0.03 |
| Factor VII | 50,000 | 0.5 | 0.01 |
| Factor VIII | 330,000 | 0.1 | 0.0003 |
| Factor IX | 56,000 | 5 | 0.08928 |
| Factor X | 58,800 | 8 | 0.13605 |
| Factor XI | 160,000 | 5 | 0.031 |
| Factor XII | 80,000 | 30 | 0.375 |
| Factor XIII | 320,000 | 10 | 0.03125 |
| Protein C | 62,000 | 4 | 0.0645 |
| Protein S | 69,000 | 10(free) | 0.1449 |
| Protein Z | 62,000 | 2.2 | 0.0355 |
| Prekallikrein | 66,000 | 50 | 0.5814 |
| HK | 110,000 | 70 | 0.6363 |
| Fibronectin | 450,000 | 300 | 0.6667 |
| Antithrombin III | 68,000 | 290 | 5 |
| Plasminogen | 90,000 | 216 | 2.4 |
| Urokinase | 60,000 | 0.1 | 0.001887 |
| Heparin Cofactor II | 66,000 | 90 | 1.3638 |
| Alpha, Antiplasmin | 63,000 | 60 | 0.9624 |
| Protein C Inhibitor | 57,000 | 4 | 0.0404 |
| Alpha ₂ -Macroglobulin | 725,000 | 2100 | 2.8666 |

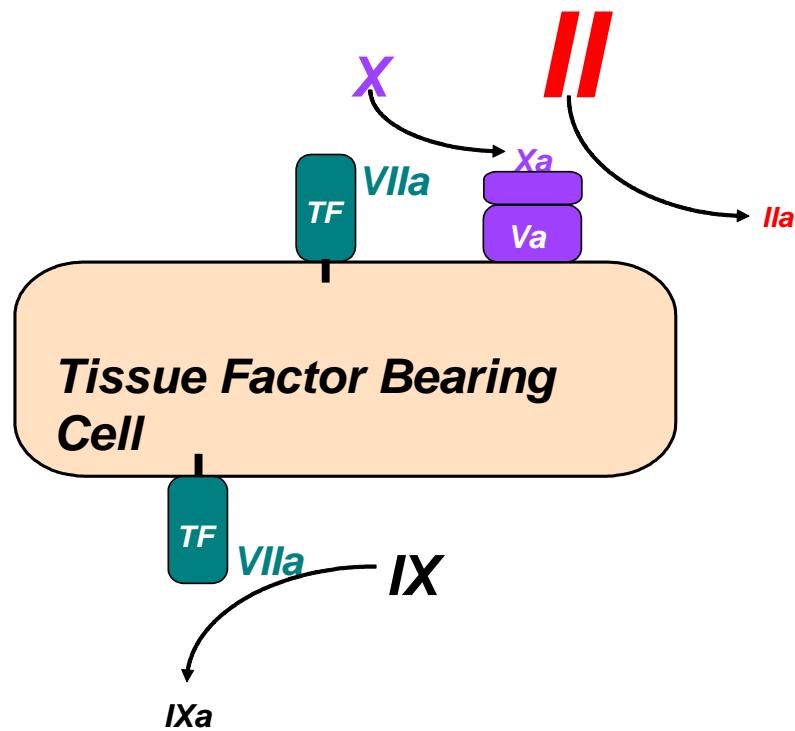
Fibrinolysis



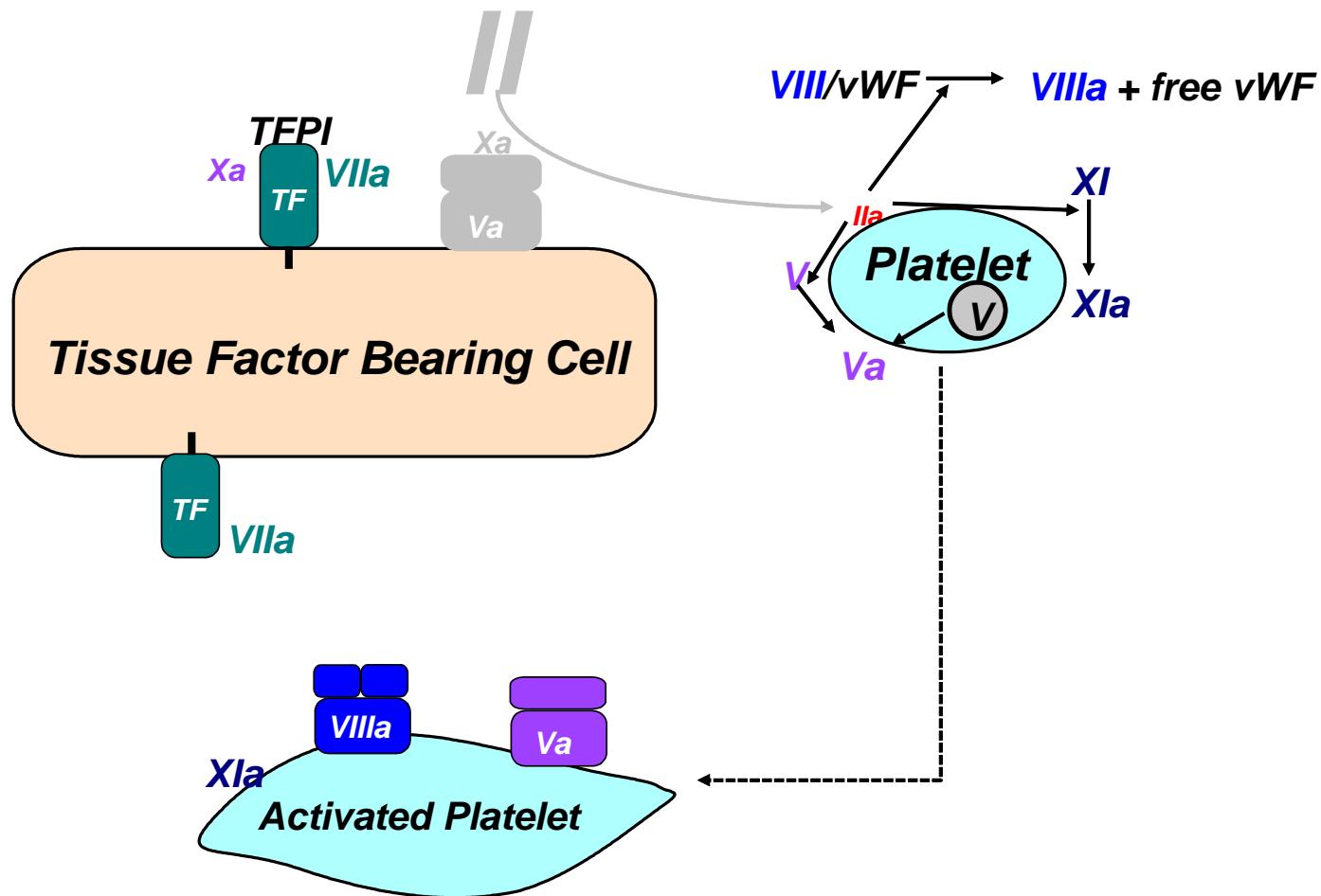
Inhibitors in black

* Thrombophilia gene mutation

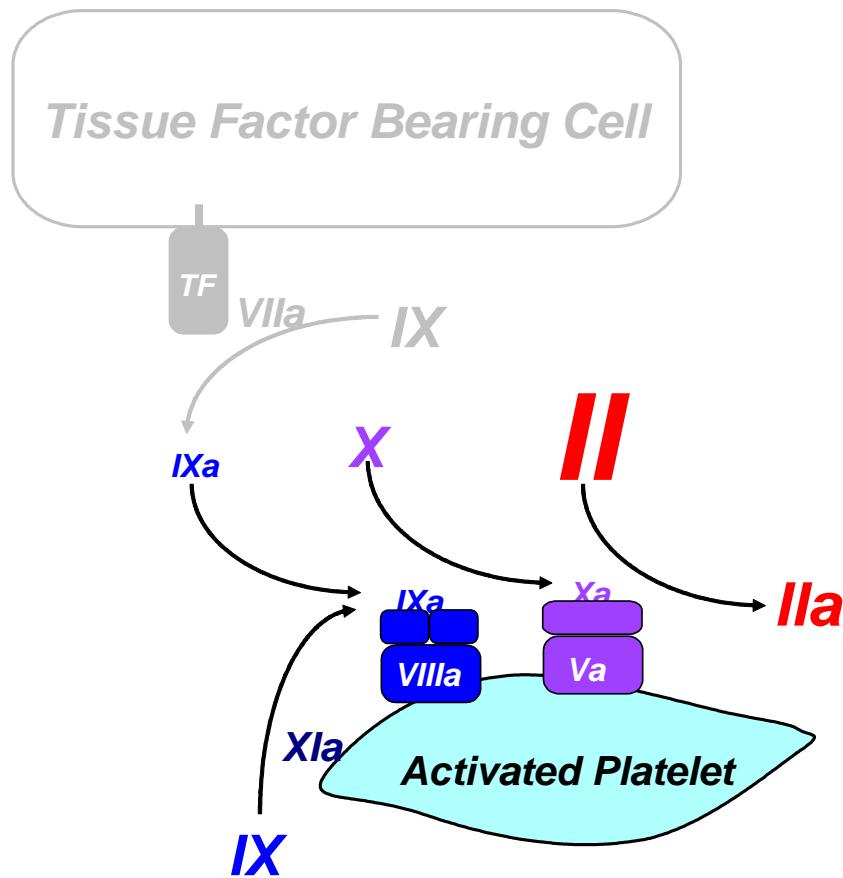
“Cell based model of hemostasis”



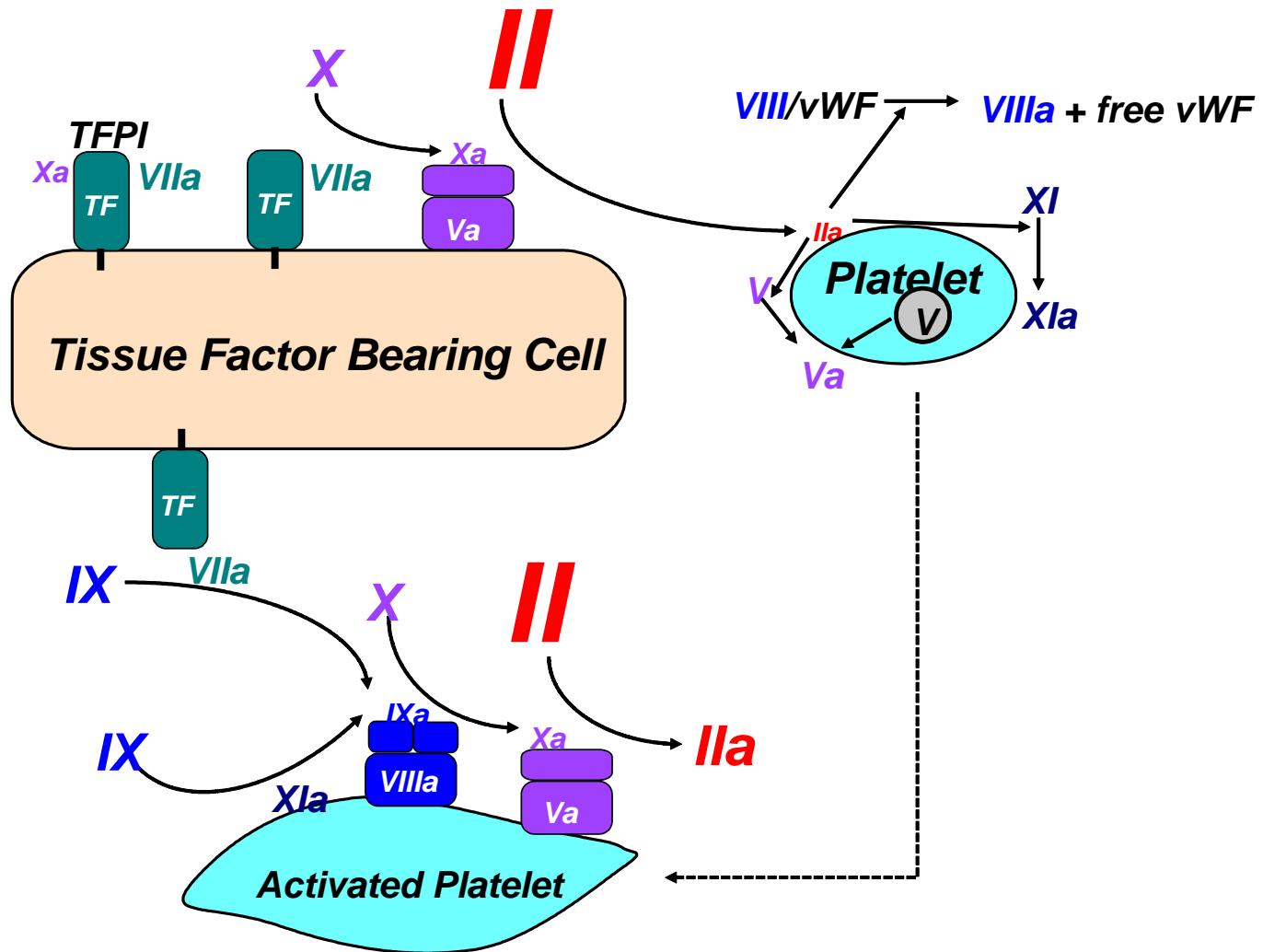
“Cell based model of hemostasis”



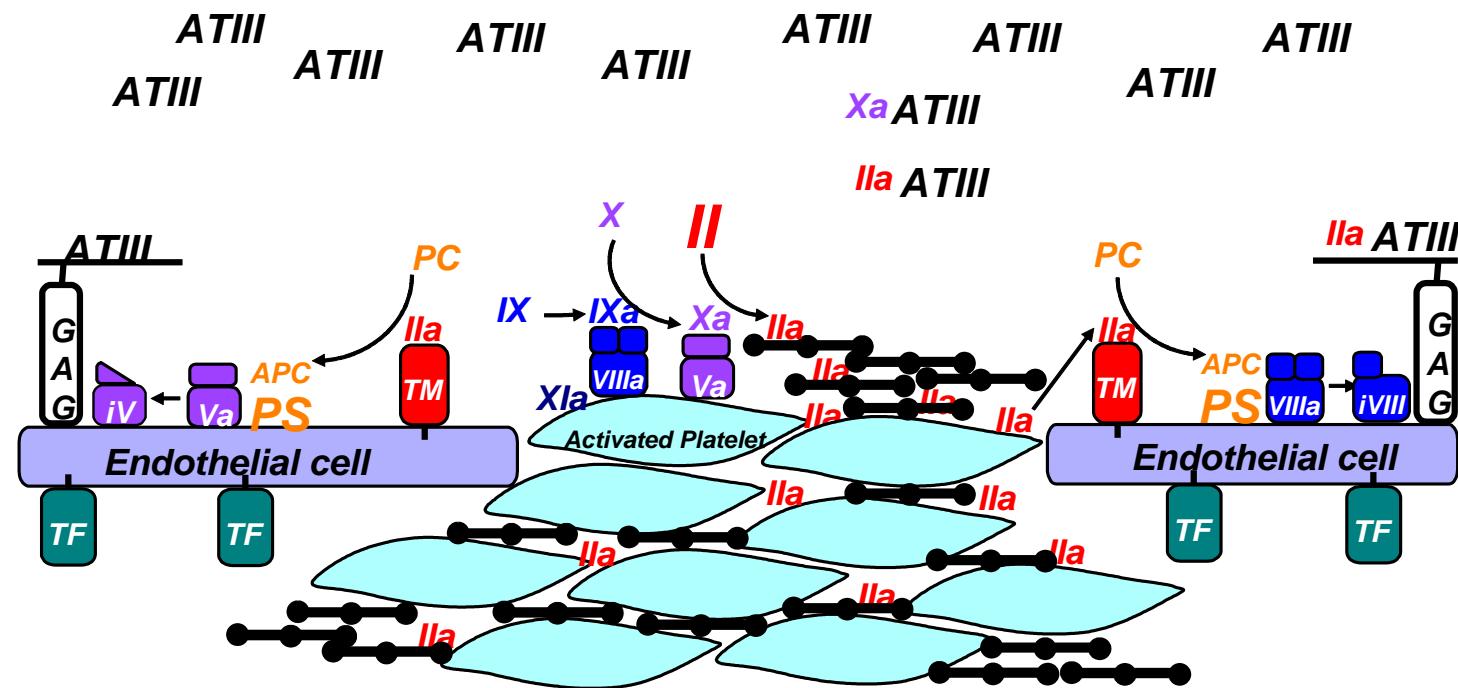
“Cell based model of hemostasis”

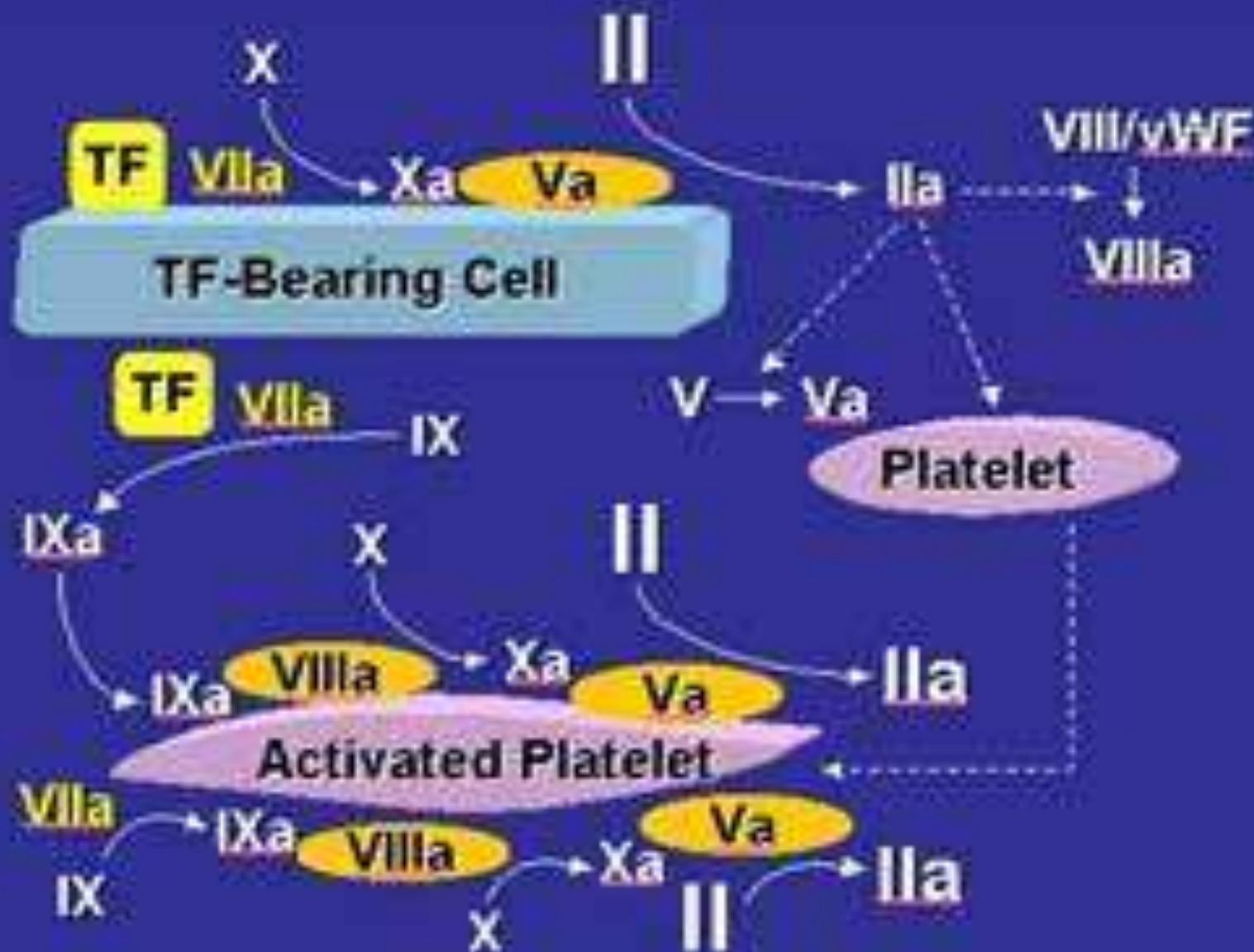


“Cell based model of hemostasis”



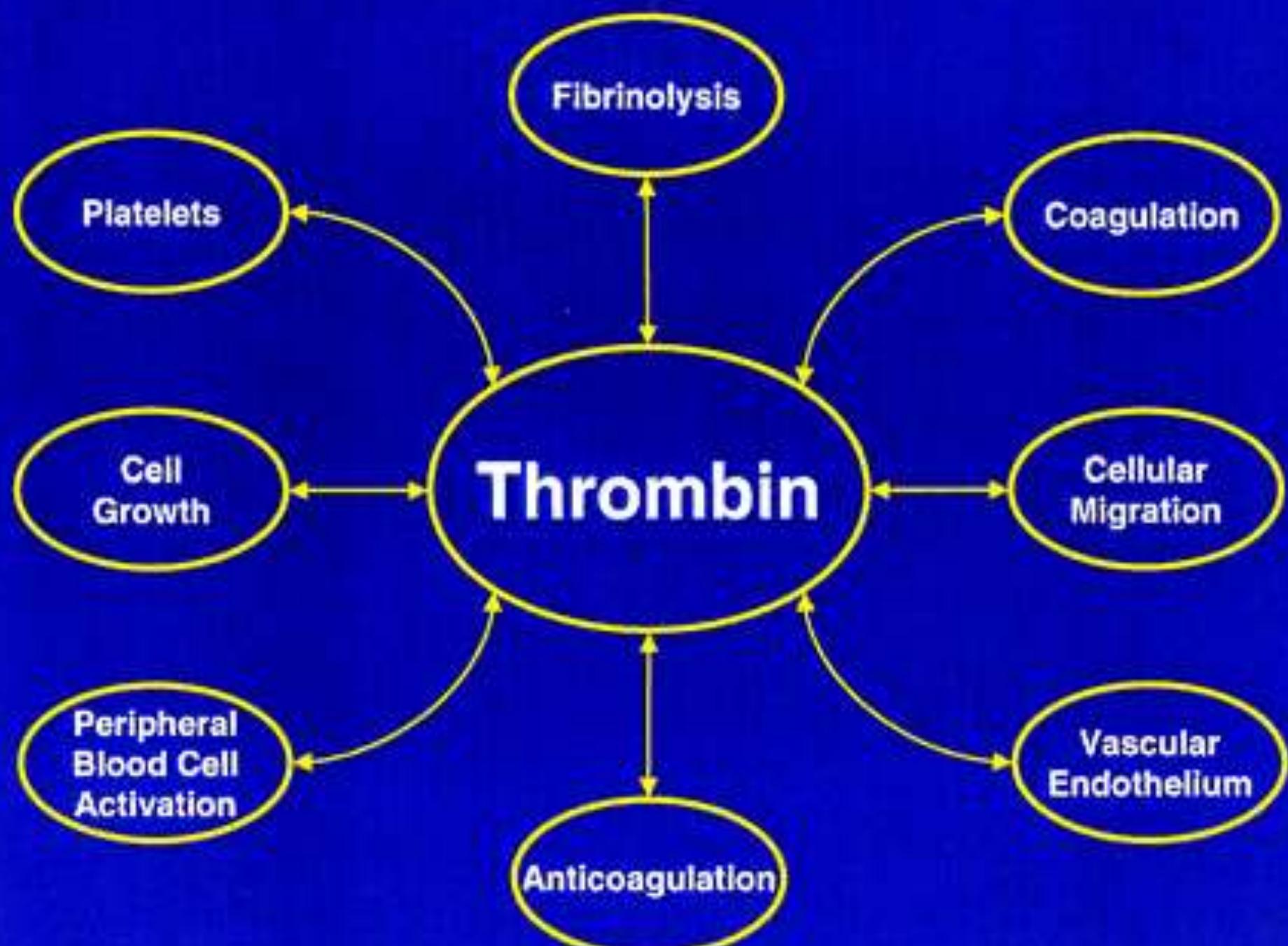
“Cell based model of hemostasis”





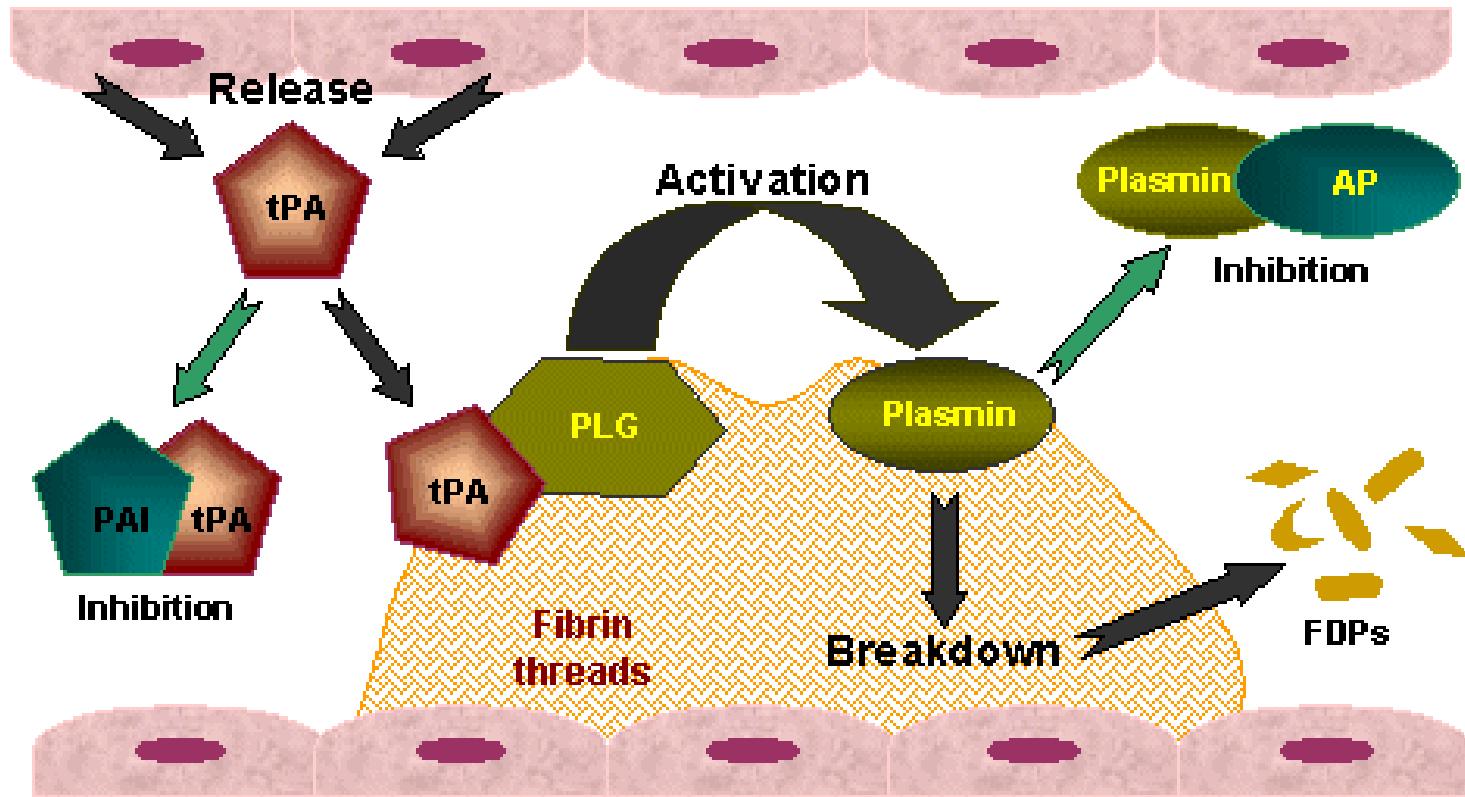
Reproduced with permission from:

Hoffman M, et al. *Blood Coagul Fibrinolysis*. 1993;9(suppl 1):S81-S85.



Fiziologija normalne hemostaze

FIBRINOLIZA: ograničava širenje tromba van mesta ozlede, dovodi do njegove lize i zarastanja rane



TROMBOZA

Tromboza (arterijska ili venska) nastaje kao kombinacija faktora tzv. Virchow-ljevog trijasa:

- ▲ Tok krvi (staza ili turbulencija)
- ▲ Zid krvnog suda (vaskularne i endotelne funkcije)
- ▲ Sastav krvi (poremećena ravnoteža izmedju koagulacije i fibrinolize)

ARTERIJSKA TROMBOZA

PATOGENEZA: Ateromatozno oštećenje endotela sa adhezijom trombocita i stvaranjem fibrina. Relativna neravnoteža izmedju stvaranja proagregatornog tromboksana A₂ i antiagregatornog prostaciklina može dovesti do tromboze

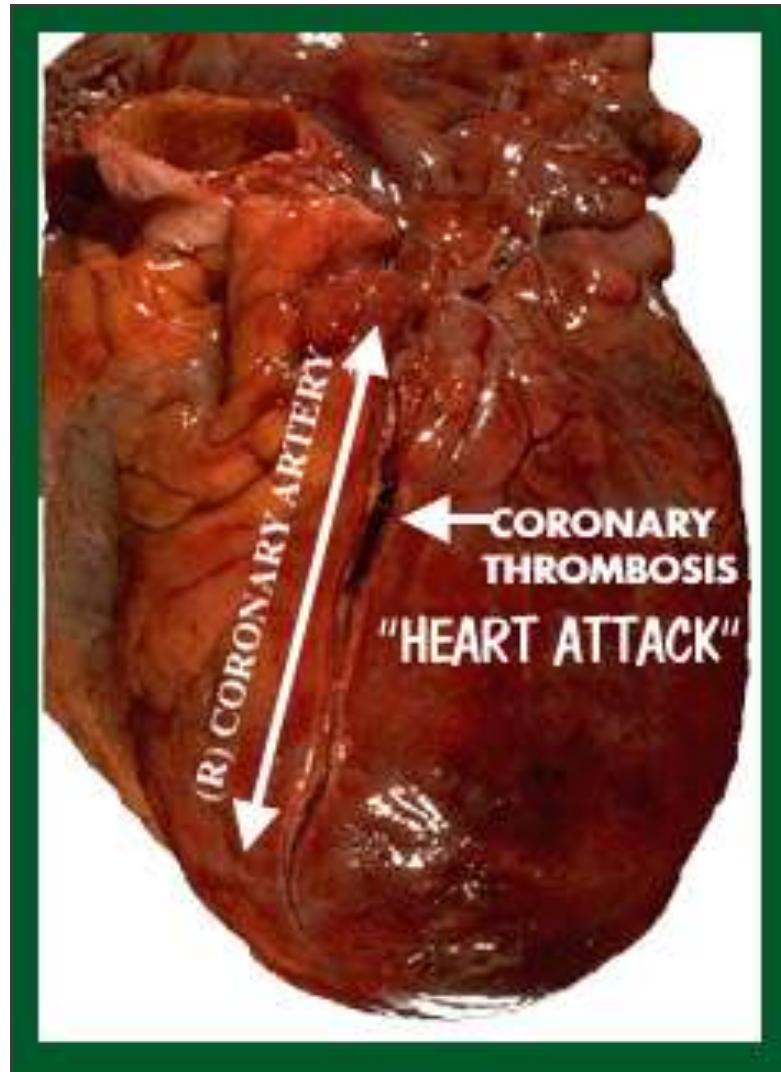
ASOCIJACIJE: Hipertenzija, ateroskleroza, hiperlipidemija, diabetes mellitus, policitemija, pušenje, lupus antikoagulans, hiperhomocisteinemija, porodična

KLINIČKA SLIKA: Ishemijska bolest srca, cerebrovaskularne bolesti, bolesti perifernih arterija

DIJAGNOZA: Kliničko ispitivanje, arteriografija, specifično

PREVENCIJA I TERAPIJA: Antiagregaciona, antikoagulantna, tromboliza

ARTERIJSKA TROMBOZA



VENSKA TROMBOZA

PATOGENEZA: Povećana lokalna produkcija trombina sa taloženjem fibrina i agregacijom trombocita u krvnim sudovima sa sporijim protokom bez oštećenja endotela.

ASOCIJACIJE: Imobilizacija, trauma, gojaznost, trudnoća, mijeloproliferativne bolesti, malignitet, oralni kontraceptivi, lupus antikoagulans, hiperhomocisteinemija, porodična

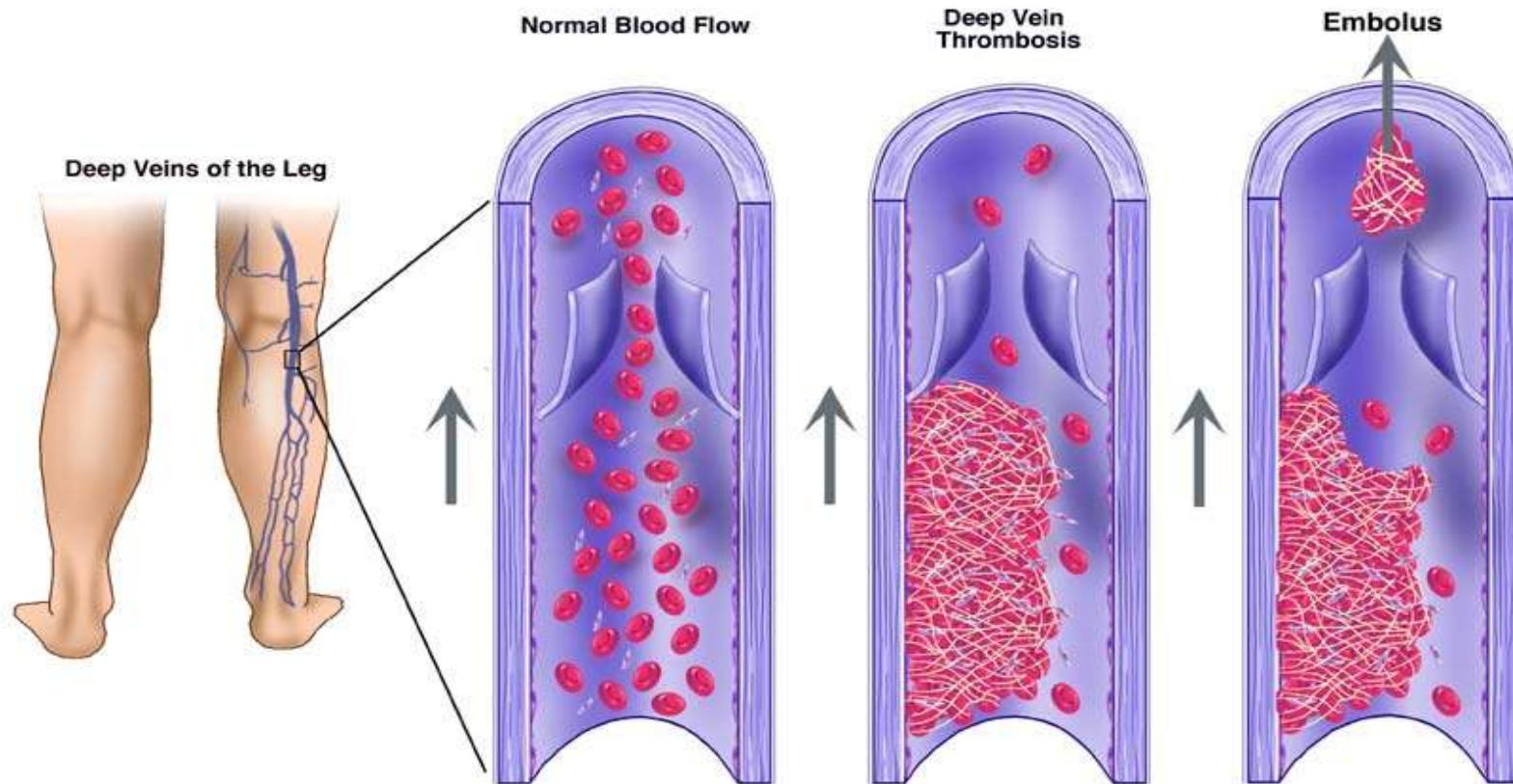
KLINIČKA SLIKA: Duboka venska tromboza, embolija pluća

DIJAGNOZA: Kliničko ispitivanje, dopler ultrazvuk, venografija, CT, D-dimer

PREVENCIJA I TERAPIJA: Antikoagulantna, trombolitička

VENSKA TROMBOZA

Deep Vein Thrombosis (DVT)

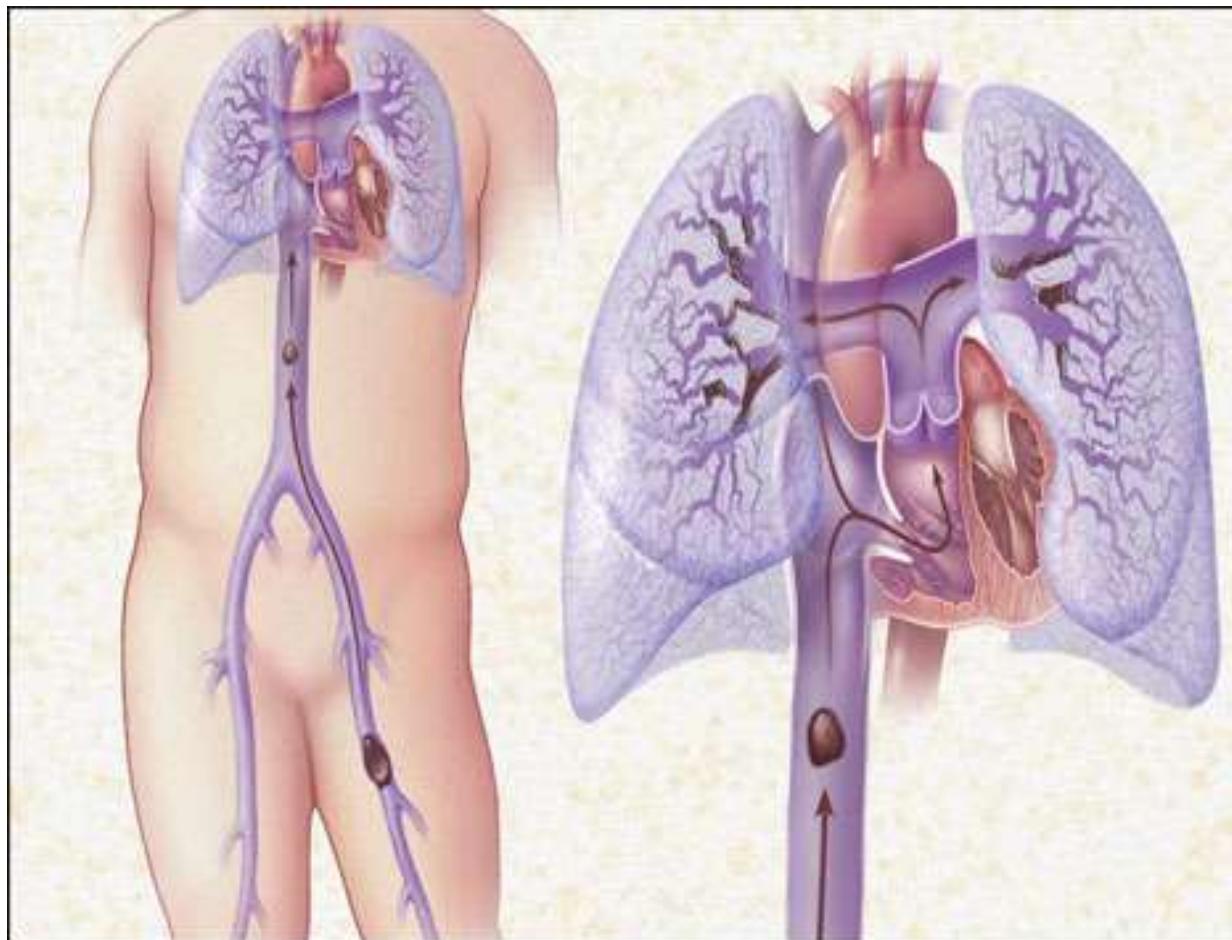




© ADAM



VENSKI TROMBOEMBOLIZAM



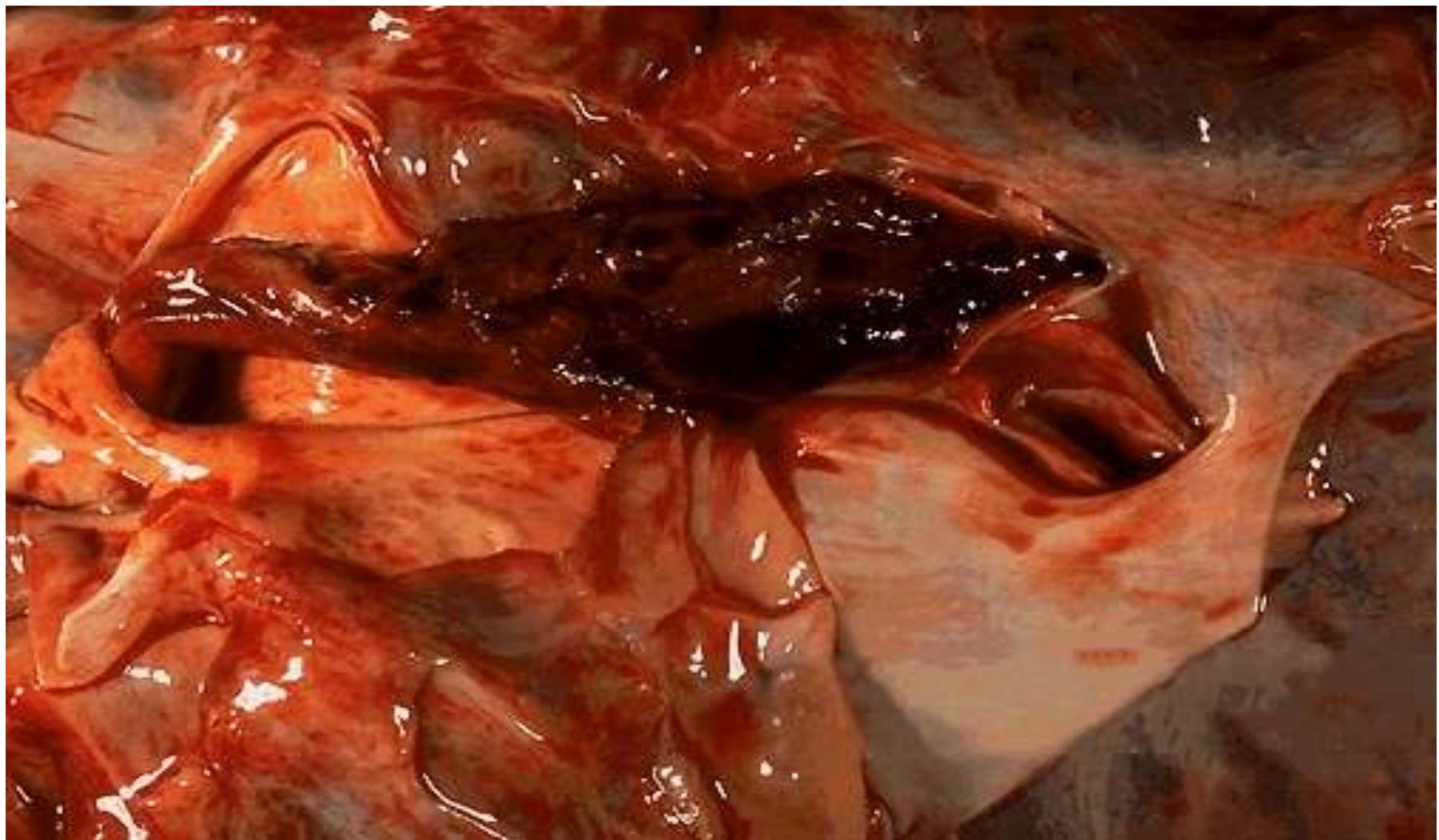
If fragments of a deep vein thrombosis break loose, they can be carried to the lungs, blocking blood flow. This is called a pulmonary embolism, and it can be fatal.

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EMBOLIJA PLUĆA



EMBOLIJA PLUĆA



Check lista DVT/PE

- PRIJEM (URGENTNI CENTAR)
- Klinika: Wells skor
- Dijagnostika: Ultrazvuk-dopler alt CT, angiografija (izuzetno)/spiral CT, pulmonalna angiografija (izuzetno)
- Ispitivanja: EKG, UZ srca, gasne analize (samo kod PE)
- Analize: D-dimer, Hb, Tr, PT-INR, APTT, S-kreatinin
- Terapija: Fragmin (200 IU/kg), preklapanje sa Warfarinom (4, 4, 3, 2?), kompresiona čarapa klasa I

- AMBULANTA ZA TROMBOZE
- Analize: PT-INR dnevno APTT kod standardnog heparina (ne Fragmina); 4-i dan Hb, Tr
- Puna pisana informacija o Warfarinu, Warfarin pločica

- OPŠTA PRAKSA/ANTIKOAGULNTNA AMBULANTA
- Kontrola PT-INR-a (4 nedelje) kompresiona čarapa klasa II (6-12 meseci)



kompresiona čarapa klasa I



kompresiona čarapa klasa II



TROMBOFILIJА

Trombofilija je urodjena ili nasledna sklonost trombozama usled hiperkoagulabilnosti

| HYPERCOAGULABLE STATE | CHARACTERISTIC SITES OF THROMBOSIS | REFERENCE |
|---|---|--|
| Congenital | | |
| Deficiency of protein C | Deep veins of legs | Rosenberg and Aird, ¹ Greaves and Preston, ² Nachman and Silverstein, ³ Macik and Ortel, ⁴ Thomas and Roberts, ⁵ De Stefano et al., ⁶ Martinelli et al. ⁷ |
| Deficiency of protein S | Deep veins of legs | Rosenberg and Aird, ¹ Greaves and Preston, ² Nachman and Silverstein, ³ Macik and Ortel, ⁴ Thomas and Roberts, ⁵ De Stefano et al., ⁶ Martinelli et al. ⁷ |
| Deficiency of antithrombin III Heterozygous | Deep veins of legs | Rosenberg and Aird, ¹ Greaves and Preston, ² Nachman and Silverstein, ³ Macik and Ortel, ⁴ Thomas and Roberts, ⁵ De Stefano et al., ⁶ Martinelli et al. ⁷ |
| Homozygous for mutation of heparin-binding domain | Deep veins and arteries | Boyer et al., ⁸ Finazzi et al., ⁹ Chowdhury et al., ¹⁰ Okajima et al. ¹¹ |
| Presence of factor V Leiden | Deep veins of legs and brain, coronary arteries* | Martinelli et al., ¹² Price and Ridker, ¹³ Rosendaal et al. ^{14*} |
| Presence of prothrombin G20210A mutation | Deep veins of legs and brain, coronary and cerebral arteries† | Martinelli et al., ¹² Margaglione et al., ¹⁵ Reuner et al., ¹⁶ De Stefano et al., ¹⁷ Arruda et al., ¹⁸ Rosendaal et al. ¹⁹ |
| Acquired | | |
| Paroxysmal nocturnal hemoglobinuria | Portal and hepatic veins | Dilawari et al., ²⁰ Hillmen et al., ²¹ Socie et al. ²² |
| Mycloproliferative diseases | Portal and hepatic veins | Dilawari et al. ²⁰ |
| Antiphospholipid antibody syndrome | Arteries and veins | Asherson et al., ²³ Khamashita et al., ²⁴ Finazzi et al. ²⁵ |
| Warfarin-induced skin necrosis | Subcutaneous microvessels | Comp et al. ²⁶ |
| Thrombotic thrombocytopenic purpura | All microvessels, with the exception of those of the liver and lung | Ridolfi and Bell, ²⁷ Asada et al., ²⁸ Ruggenenti and Remuzzi ²⁹ |

*Most studies have not confirmed an association between factor V Leiden and arterial disease. The risk of ischemic heart disease may be limited to young women who smoke.

†The association between the prothrombin G20210A mutation and arterial disease requires confirmation in additional studies.

NASLEDNE TROMBOFILIJE

APC REZISTENCIJA

FV Leiden (Arg506Gln), FV Cambridge (Arg306Thr), FV Hong Kong (Arg306Gly)

FV Leiden 20-40% DVT, 5-7% populacije, u Skandinaviji do 10% heterozigota

NEDOSTATAK PC

1% DVT, 1/200 - 1/300 u populaciji

Tip I – sniženje i antigena i aktivnosti

Tip II - normalan antigen, niska aktivnost (funkcionalna)

NEDOSTATAK PS

1% svih tromboza

Tip I – nizak totalni PS uz nizak slobodni PS i aktivnost

Tip II - normalan PS antigen uz nizak slobodni PS i aktivnost

Tip III – porast vezanog PS uz nizak slobodni

DEFICIJENCIJA TROMBOMODULINA?

NASLEDNE TROMBOFILIE

NEDOSTATAK AT

5% svih trombotskih epizoda kod mlađih od 40 godina

1/2000 - 1/5000 u populaciji

Tip I – sniženje i antigaena i aktivnosti

Tip II - normalan antigen, niska aktivnost (funkcionalna)

PROTROMBIN GEN MUTACIJA 20210

5-7% svih tromboza

1% opšte populacije

DISFIBRINOGENEMIJA

NEDOSTATAK FXII ?

HIPERHOMOCISTEINEMIJA ?

nasledna (MTHFR polimorfizam) ili stečena

10% tromboza ?

5% populacije

terapija folnom kiselinom

LABORATORIJSKA DIJAGNOZA TROMBOFILIIA

KOGA TESTIRATI

- ♦ Pacijenti mlađi od 50 godina sa prvom VTE
- ♦ Pacijenti stariji od 50 godina sa jasnim naslednjim faktorom sa prvom VTE
- ♦ Bez obzira na godine kod ponovljene tromboze bez jasnog uzroka
- ♦ Rekurentni pobačaji

LABORATORIJSKA DIJAGNOZA TROMBOFILIIA

KADA TESTIRATI

- ♦ Po pravilu 4 nedelje nakon prestanka Warfarina
- ♦ Većinu analiza moguća i u toku akutne faze (akutna faza utiče na FVIII, ostali faktori?)
- ♦ Warfarin utiče na LA (LMWH takođe)
- ♦ PC, PS u odnosu na PT-INR?!

LABORATORIJSKA DIJAGNOZA TROMBOFILIIJA

ŠTA TESTIRATI

- ◆ Kod poznatog poremećaja (nasledno) najpre taj parametar
- ◆ Trombofilija paket

LABORATORIJSKA DIJAGNOZA TROMBOFILIIA

RUTINSKI TESTOVI

- APC rezistencija (modifikovani aPTT test)
- PC funkcionalni test
- PS funkcionalni test (slobodni)
- AT funkcionalni test
- Lupus antikoagulans (LA)
- Antifosfolipidna antitela (APA)
- FVIII
- FV Leiden mutacija (G1691A)
- protrombin mutacija(G20210A)
- homocistein

POTVRDNI TESTOVI

- PC antigen
- PS antigen
- AT antigen

DODATNI TESTOVI

- plazminogen aktivnost i antigen
- t-PA
- HCII
- disfibrinogenemija (TT)
- FXII

DOPUNSKI TESTOVI

- TM i MTHFR polimorfizam

Stämpel Auskündiger/Mottagare samt Patientens Personnr./Namn

OBST: Test får ej göras i följet avsett för bestämmningar.

Markera provtagningsdag. Prov taget kl. 09 Läkarkod samt lämna till vårt laboratorium.



Markera i avsättda ovaler med ett tjockt streck. Använd kulispest- eller blyertspenna.

EXEMPEL:

Läkarkod 98123 markera

| Färg prövad | Typ av m |
|-------------|---------------------------------|
| Blå | Na-Citrat OEGI gjord i S re |
| Lila | EDTA |
| Självgrön | Li-biphenol med gel |
| Gul | Utan tillägg men med gel |
| | spårar hög lila färg till 73130 |

KOAGULATION ANVISNING

Ramissen innehåller endast specialavgränsningskriterier

Screeningsanalysen (NPF-nd, PK-mit.) berättas på remiss "Klack kom Almän".

se även provtagningsanvisningar på www.karolinska.se/lat.

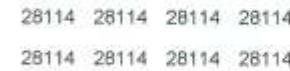
Ustedes de p a remissen sanci nica an醕almente. Sintetizan esto en la medida m醩ica.

Konkurrensanalyser tillämpas
Vid frågor rörande ej angivna analyser eller vid bevisar om vad av analyser eller

Utredningsförslagens omfattning, Præagiung

| Allmän blödningstestning | rör (pröpp) | Vad är Trombos | rör (pröpp) |
|--|----------------------------------|--|------------------------|
| Rörmars Speciellkoagulation vWF Ag, vWF BCoF akt. F VIII, F IX, PAI-1 | 2 till 2 till | Rörmars Speciellkoagulation F VIII, Protein E, fibrinogen C (aktiv) | 2 till 2 till |
| Kapillärblödning | Slipettur | Luzus antikoagulator | |
| Rörmars Klinisk hemi Allmän TPK, APTT-hgt, PK, Fibrinogen CRP | 1 till, till 1 luftigt | DNA: Faktor V 1691G-A Faktor II 20210G-A | 1 till 1 till |
| Anterioti Trombos | rör (pröpp) | Rörmars Klinisk hemi Allmän CRF, Antikroton Homocystein | 1 luftigt 1 luftigt |
| Rörmars Speciellkoagulation F VIII, VIII-1, Luzus antikoagulator | 2 till | Rörmars kromatografi Lipoproteinlipoprotéiner | 1 gal |
| Rörmars Klinisk hemi Allmän Fibrinogen, Antikroton CRP, Lipoprotein (a) Homocystein | 1 till 1 luftigt 1 luftigt | Hereditet för venös trombos | rör (pröpp) |
| Rörmars kromatografi Kardiolipinantikroppar | 1 gal | Rörmars Speciellkoagulationen Protein E, fibrinogen C (aktiv) | 1 till 1 till |
| | | DNA: Faktor V 1691G-A Faktor II 20210G-A | 1 till 1 till |
| | | Rörmars Klinisk hemi Allmän Antikroton | 1 till |

TAG RÄTT ETIKETT TILL RÄTT RÖR!



Venös Trombos rör (propp)

| | |
|--|---|
| <i>Remiss Specialkoagulation</i> F VIII, Protein S, fritt, Protein C (enz) Lupus antikoagulans | 2 blå |
| DNA: Faktor V 1691G-A Faktor II 20210G-A | 1 lila <small>ej centrifugerat</small> |
| <i>Remiss Klinisk kemi Allmän</i> CRP, Antitrombin Homocystein | 1 ljusgrön, 1 blå 1 ljusgrön |
| <i>Remiss Immunologi</i> Kardiolipinantikroppar | 1 gul |

Stämpta Avsändare/Mottagare samt
Patientens Personnummer.

OBST Text får ej gör ner i fältet avsett
för beställningar.

Markera provtagningsdag. Prov taget ki
av Läkarkod samt sätigt Ni vill meddela
laboratoriet.



Markera i avsedda rutor med ett
tjockt streck. Använd kulepet- eller
blyertspenna.

EXEMPEL:

Läkarkod 98123 markerat:

| Läkarkod | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 | 41 | 42 | 43 | 44 | 45 | 46 | 47 | 48 | 49 | 50 | 51 | 52 | 53 | 54 | 55 | 56 | 57 | 58 | 59 | 60 | 61 | 62 | 63 | 64 | 65 | 66 | 67 | 68 | 69 | 70 | 71 | 72 | 73 | 74 | 75 | 76 | 77 | 78 | 79 | 80 | 81 | 82 | 83 | 84 | 85 | 86 | 87 | 88 | 89 | 90 | 91 | 92 | 93 | 94 | 95 | 96 | 97 | 98 | 99 | 100 | 101 | 102 | 103 | 104 | 105 | 106 | 107 | 108 | 109 | 110 | 111 | 112 | 113 | 114 | 115 | 116 | 117 | 118 | 119 | 120 | 121 | 122 | 123 | 124 | 125 | 126 | 127 | 128 | 129 | 130 | 131 | 132 | 133 | 134 | 135 | 136 | 137 | 138 | 139 | 140 | 141 | 142 | 143 | 144 | 145 | 146 | 147 | 148 | 149 | 150 | 151 | 152 | 153 | 154 | 155 | 156 | 157 | 158 | 159 | 160 | 161 | 162 | 163 | 164 | 165 | 166 | 167 | 168 | 169 | 170 | 171 | 172 | 173 | 174 | 175 | 176 | 177 | 178 | 179 | 180 | 181 | 182 | 183 | 184 | 185 | 186 | 187 | 188 | 189 | 190 | 191 | 192 | 193 | 194 | 195 | 196 | 197 | 198 | 199 | 200 | 201 | 202 | 203 | 204 | 205 | 206 | 207 | 208 | 209 | 210 | 211 | 212 | 213 | 214 | 215 | 216 | 217 | 218 | 219 | 220 | 221 | 222 | 223 | 224 | 225 | 226 | 227 | 228 | 229 | 230 | 231 | 232 | 233 | 234 | 235 | 236 | 237 | 238 | 239 | 240 | 241 | 242 | 243 | 244 | 245 | 246 | 247 | 248 | 249 | 250 | 251 | 252 | 253 | 254 | 255 | 256 | 257 | 258 | 259 | 260 | 261 | 262 | 263 | 264 | 265 | 266 | 267 | 268 | 269 | 270 | 271 | 272 | 273 | 274 | 275 | 276 | 277 | 278 | 279 | 280 | 281 | 282 | 283 | 284 | 285 | 286 | 287 | 288 | 289 | 290 | 291 | 292 | 293 | 294 | 295 | 296 | 297 | 298 | 299 | 300 | 301 | 302 | 303 | 304 | 305 | 306 | 307 | 308 | 309 | 310 | 311 | 312 | 313 | 314 | 315 | 316 | 317 | 318 | 319 | 320 | 321 | 322 | 323 | 324 | 325 | 326 | 327 | 328 | 329 | 330 | 331 | 332 | 333 | 334 | 335 | 336 | 337 | 338 | 339 | 340 | 341 | 342 | 343 | 344 | 345 | 346 | 347 | 348 | 349 | 350 | 351 | 352 | 353 | 354 | 355 | 356 | 357 | 358 | 359 | 360 | 361 | 362 | 363 | 364 | 365 | 366 | 367 | 368 | 369 | 370 | 371 | 372 | 373 | 374 | 375 | 376 | 377 | 378 | 379 | 380 | 381 | 382 | 383 | 384 | 385 | 386 | 387 | 388 | 389 | 390 | 391 | 392 | 393 | 394 | 395 | 396 | 397 | 398 | 399 | 400 | 401 | 402 | 403 | 404 | 405 | 406 | 407 | 408 | 409 | 410 | 411 | 412 | 413 | 414 | 415 | 416 | 417 | 418 | 419 | 420 | 421 | 422 | 423 | 424 | 425 | 426 | 427 | 428 | 429 | 430 | 431 | 432 | 433 | 434 | 435 | 436 | 437 | 438 | 439 | 440 | 441 | 442 | 443 | 444 | 445 | 446 | 447 | 448 | 449 | 450 | 451 | 452 | 453 | 454 | 455 | 456 | 457 | 458 | 459 | 460 | 461 | 462 | 463 | 464 | 465 | 466 | 467 | 468 | 469 | 470 | 471 | 472 | 473 | 474 | 475 | 476 | 477 | 478 | 479 | 480 | 481 | 482 | 483 | 484 | 485 | 486 | 487 | 488 | 489 | 490 | 491 | 492 | 493 | 494 | 495 | 496 | 497 | 498 | 499 | 500 | 501 | 502 | 503 | 504 | 505 | 506 | 507 | 508 | 509 | 510 | 511 | 512 | 513 | 514 | 515 | 516 | 517 | 518 | 519 | 520 | 521 | 522 | 523 | 524 | 525 | 526 | 527 | 528 | 529 | 530 | 531 | 532 | 533 | 534 | 535 | 536 | 537 | 538 | 539 | 540 | 541 | 542 | 543 | 544 | 545 | 546 | 547 | 548 | 549 | 550 | 551 | 552 | 553 | 554 | 555 | 556 | 557 | 558 | 559 | 560 | 561 | 562 | 563 | 564 | 565 | 566 | 567 | 568 | 569 | 570 | 571 | 572 | 573 | 574 | 575 | 576 | 577 | 578 | 579 | 580 | 581 | 582 | 583 | 584 | 585 | 586 | 587 | 588 | 589 | 590 | 591 | 592 | 593 | 594 | 595 | 596 | 597 | 598 | 599 | 600 | 601 | 602 | 603 | 604 | 605 | 606 | 607 | 608 | 609 | 610 | 611 | 612 | 613 | 614 | 615 | 616 | 617 | 618 | 619 | 620 | 621 | 622 | 623 | 624 | 625 | 626 | 627 | 628 | 629 | 630 | 631 | 632 | 633 | 634 | 635 | 636 | 637 | 638 | 639 | 640 | 641 | 642 | 643 | 644 | 645 | 646 | 647 | 648 | 649 | 650 | 651 | 652 | 653 | 654 | 655 | 656 | 657 | 658 | 659 | 660 | 661 | 662 | 663 | 664 | 665 | 666 | 667 | 668 | 669 | 660 | 661 | 662 | 663 | 664 | 665 | 666 | 667 | 668 | 669 | 670 | 671 | 672 | 673 | 674 | 675 | 676 | 677 | 678 | 679 | 680 | 681 | 682 | 683 | 684 | 685 | 686 | 687 | 688 | 689 | 690 | 691 | 692 | 693 | 694 | 695 | 696 | 697 | 698 | 699 | 700 | 701 | 702 | 703 | 704 | 705 | 706 | 707 | 708 | 709 | 710 | 711 | 712 | 713 | 714 | 715 | 716 | 717 | 718 | 719 | 720 | 721 | 722 | 723 | 724 | 725 | 726 | 727 | 728 | 729 | 730 | 731 | 732 | 733 | 734 | 735 | 736 | 737 | 738 | 739 | 740 | 741 | 742 | 743 | 744 | 745 | 746 | 747 | 748 | 749 | 750 | 751 | 752 | 753 | 754 | 755 | 756 | 757 | 758 | 759 | 760 | 761 | 762 | 763 | 764 | 765 | 766 | 767 | 768 | 769 | 770 | 771 | 772 | 773 | 774 | 775 | 776 | 777 | 778 | 779 | 770 | 771 | 772 | 773 | 774 | 775 | 776 | 777 | 778 | 779 | 780 | 781 | 782 | 783 | 784 | 785 | 786 | 787 | 788 | 789 | 790 | 791 | 792 | 793 | 794 | 795 | 796 | 797 | 798 | 799 | 800 | 801 | 802 | 803 | 804 | 805 | 806 | 807 | 808 | 809 | 810 | 811 | 812 | 813 | 814 | 815 | 816 | 817 | 818 | 819 | 820 | 821 | 822 | 823 | 824 | 825 | 826 | 827 | 828 | 829 | 830 | 831 | 832 | 833 | 834 | 835 | 836 | 837 | 838 | 839 | 840 | 841 | 842 | 843 | 844 | 845 | 846 | 847 | 848 | 849 | 850 | 851 | 852 | 853 | 854 | 855 | 856 | 857 | 858 | 859 | 860 | 861 | 862 | 863 | 864 | 865 | 866 | 867 | 868 | 869 | 860 | 861 | 862 | 863 | 864 | 865 | 866 | 867 | 868 | 869 | 870 | 871 | 872 | 873 | 874 | 875 | 876 | 877 | 878 | 879 | 880 | 881 | 882 | 883 | 884 | 885 | 886 | 887 | 888 | 889 | 880 | 881 | 882 | 883 | 884 | 885 | 886 | 887 | 888 | 889 | 890 | 891 | 892 | 893 | 894 | 895 | 896 | 897 | 898 | 899 | 900 | 901 | 902 | 903 | 904 | 905 | 906 | 907 | 908 | 909 | 910 | 911 | 912 | 913 | 914 | 915 | 916 | 917 | 918 | 919 | 920 | 921 | 922 | 923 | 924 | 925 | 926 | 927 | 928 | 929 | 930 | 931 | 932 | 933 | 934 | 935 | 936 | 937 | 938 | 939 | 940 | 941 | 942 | 943 | 944 | 945 | 946 | 947 | 948 | 949 | 950 | 951 | 952 | 953 | 954 | 955 | 956 | 957 | 958 | 959 | 960 | 961 | 962 | 963 | 964 | 965 | 966 | 967 | 968 | 969 | 960 | 961 | 962 | 963 | 964 | 965 | 966 | 967 | 968 | 969 | 970 | 971 | 972 | 973 | 974 | 975 | 976 | 977 | 978 | 979 | 980 | 981 | 982 | 983 | 984 | 985 | 986 | 987 | 988 | 989 | 980 | 981 | 982 | 983 | 984 | 985 | 986 | 987 | 988 | 989 | 990 | 991 | 992 | 993 | 994 | 995 | 996 | 997 | 998 | 999 | 1000 | 1001 | 1002 | 1003 | 1004 | 1005 | 1006 | 1007 | 1008 | 1009 | 1000 | 1001 | 1002 | 1003 | 1004 | 1005 | 1006 | 1007 | 1008 | 1009 | 1010 | 1011 | 1012 | 1013 | 1014 | 1015 | 1016 | 1017 | 1018 | 1019 | 1010 | 1011 | 1012 | 1013 | 1014 | 1015 | 1016 | 1017 | 1018 | 1019 | 1020 | 1021 | 1022 | 1023 | 1024 | 1025 | 1026 | 1027 | 1028 | 1029 | 1020 | 1021 | 1022 | 1023 | 1024 | 1025 | 1026 | 1027 | 1028 | 1029 | 1030 | 1031 | 1032 | 1033 | 1034 | 1035 | 1036 | 1037 | 1038 | 1039 | 1030 | 1031 | 1032 | 1033 | 1034 | 1035 | 1036 | 1037 | 1038 | 1039 | 1040 | 1041 | 1042 | 1043 | 1044 | 1045 | 1046 | 1047 | 1048 | 1049 | 1040 | 1041 | 1042 | 1043 | 1044 | 1045 | 1046 | 1047 | 1048 | 1049 | 1050 | 1051 | 1052 | 1053 | 1054 | 1055 | 1056 | 1057 | 1058 | 1059 | 1050 | 1051 | 1052 | 1053 | 1054 | 1055 | 1056 | 1057 | 1058 | 1059 | 1060 | 1061 | 1062 | 1063 | 1064 | 1065 | 1066 | 1067 | 1068 | 1069 | 1060 | 1061 | 1062 | 1063 | 1064 | 1065 | 1066 | 1067 | 1068 | 1069 | 1070 | 1071 | 1072 | 1073 | 1074 | 1075 | 1076 | 1077 | 1078 | 1079 | 1070 | 1071 | 1072 | 1073 | 1074 | 1075 | 1076 | 1077 | 1078 | 1079 | 1080 | 1081 | 1082 | 1083 | 1084 | 1085 | 1086 | 1087 | 1088 | 1089 | 1080 | 1081 | 1082 | 1083 | 1084 | 1085 | 1086 | 1087 | 1088 | 1089 | 1090 | 1091 | 1092 | 1093 | 1094 | 1095 | 1096 | 1097 | 1098 | 1099 | 1090 | 1091 | 1092 | 1093 | 1094 | 1095 | 1096 | 1097 | 1098 | 1099 | 1100 | 1101 | 1102 | 1103 | 1104 | 1105 | 1106 | 1107 | 1108 | 1109 | 1100 | 1101 | 1102 | 1103 | 1104 | 1105 | 1106 | 1107 | 1108 | 1109 | 1110 | 1111 | 1112 | 1113 | 1114 | 1115 | 1116 | 1117 | 1118 | 1119 | 1110 | 1111 | 1112 | 1113 | 1114 | 1115 | 1116 | 1117 | 1118 | 1119 | 1120 | 1121 | 1122 | 1123 | 1124 | 1125 | 1126 | 1127 | 1128 | 1129 | 1120 | 1121 | 1122 | 1123 | 1124 | 1125 | 1126 | 1127 | 1128 | 1129 | 1130 | 1131 | 1132 | 1133 | 1134 | 1135 | 1136 | 1137 | 1138 | 1139 | 1130 | 1131 | 1132 | 1133 | 1134 | 1135 | 1136 | 1137 | 1138 | 1139 | 1140 | 1141 | 1142 | 1143 | 1144 | 1145 | 1146 | 1147 | 1148 | 1149 | 1140 | 1141 | 1142 | 1143 | 1144 | 1145 | 1146 | 1147 | 1148 | 1149 | 1150 | 1151 | 1152 | 1153 | 1154 | 1155 | 1156 | 1157 | 1158 | 1159 | 1150 | 1151 | 1152 | 1153 | 1154 | 1155 | 1156 | 1157 | 1158 | 1159 | 1160 | 1161 | 1162 | 1163 | 1164 | 1165 | 1166 | 1167 | 1168 | 1169 | 1160 | 1161 | 1162 | 1163 | 1164 | 1165 | 1166 | 1167 | 1168 | 1169 | 1170 | 1171 | 1172 | 1173 | 1174 | 1175 | 1176 | 1177 | 1178 | 1179 | 1170 | 1171 | 1172 | 1173 | 1174 | 1175 | 1176 | 1177 | 1178 | 1179 | 1180 | 1181 | 1182 | 1183 | 1184 | 1185 | 1186 | 1187 | 1188 | 1189 | 1180 | 1181 | 1182 | 1183 | 1184 | 1185 | 1186 | 1187 | 1188 | 1189 | 1190 | 1191 | 1192 | 1193</ |
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Hereditet för venös trombos rör (propp)

| | |
|---|-----------------------------------|
| <i>Remiss Specialkoagulation</i> Protein S, fritt, Protein C (enz) | 1 blå |
| DNA: Faktor V 1691G-A Faktor II 20210G-A | 1 lila <i>ej centrifugeras</i> |
| <i>Remiss Klinisk kemi Allmän</i> Antitrombin | 1 blå |

Stämpel Ausländer/Mittagsgäste samt Patientens Personnr./Name

OBST: Test får ej göras i följet avsett för bestämmningar.

Markera provtagningsdag. Prov taget kl. av Läkarkod samt sätta till att ni vill meddela laboratoriet.



Markera i avsedda områden med en tjockt streck. Använd kläppets- eller blyertsspenna.

EXEMPEL:

Likhedal 99123 mextyp

| Färg/typ | Typ av n. |
|----------|---|
| Blå | Na-Citrat OEGI għandek il-rei |
| Lila | EDTA |
| Ljusgrön | Li-heparin med gel |
| Għaliex | Uħien il-kollha minn med gel sugħiex kollha tħalli tħalli 88 817 731 |

KOAGULATION ANVISNING

Ramkissen innehåller endast specialkoagulationsaktivator

Screeninganalysen (APT-od, PK mfl.) berättas på renissa "Klinick kom Almän".

se även priviligeringsutvärderingar på www.kaminska.se/lis

Udover de på højsædet angivne analytiske felter blev et antal modre faktorer

Vid frågor om utvärderingar av angivna analyser eller vid frågor om vad av analyser är tillgängliga kan du kontakta oss via e-post till Statisticalcalculator@sf.se eller telefon 08-517 73320.

Utredningsförslagens omfattning. Provtagning

| Allmän blödningsutredning | rör (pröpp) | Venös Trombos | rör (pröpp) |
|----------------------------------|--------------------|---|----------------|
| Rörmars Specialektroagulation | | Rörmars Specialaggregation | |
| vWF Ag, vWF BCU-fakt. | 2 titr | F VIII, Protein E, fibrin, Protein C (arteri) | 2 titr |
| F VIII, F IX, PAI-1 | | Lupus antikongjugat | |
| Kapillärblödning | Surgicutt | DNA: Factor V 1691G-A | 1 titr |
| | | Faktor II 20210G-A | 1 titr |
| Rörmars Klinisk kemt Alkohol | | | |
| TBK (0-100), PK, Fibrinogen | titr, 1 titr | Femors Klinisk kemt Alkohol | 1 titr, 1 titr |
| ATF | 1 (μg/ml) | CRP, Antitrombin | 1 (μg/ml) |
| | | Hemocystein | 1 (μg/ml) |
| Arteriell Trombos | rör (pröpp) | Rörmars Immunolog! | |
| Rörmars Specialektroagulation | | Kardiolipinantikroppar | 1 gal |
| F VIII, F I: Lupus antikongjugat | 2 titr | | |
| | | | |
| Rörmars Klinisk kemt Alkohol | | | |
| Fibrinogen, Antitrombin | 1 titr | | |
| CRP, Lepraminn (la) | 1 (μg/ml) | | |
| Homocystein | 1 (μg/ml) | | |
| Rörmars Immunolog! | | | |
| Kardiolipinantikroppar | 1 gal | | |

TAG RÄTT ETIKETT TILL RÄTT RÖR!

28114 28114 28114 28114

28114 28114 28114 28114



Arteriell Trombos rör (propp)

| | |
|---|-----------------------------------|
| <i>Remiss Specialkoagulation</i> F VIII, PAI-1, Lupus antikoagulans | 2 blå |
| <i>Remiss Klinisk kemi Allmän</i> Fibrinogen, Antitrombin CRP, Lipoprotein (a) Homocystein | 1 blå 1 ljusgrön 1 ljusgrön |
| <i>Remiss Immunologi</i> Kardiolipinantikroppar | 1 gul |

LABORATORIJSKA DIJAGNOZA TROMBOFILIIA

| Trombofilija | Opšta prevalenca (%) | Prevalenca kod DVT/PE (%) | Porast rizika (puta) | Rizik od recidiva | Testiranje za vreme warfarina |
|-----------------------|----------------------|---------------------------|----------------------|-------------------|-------------------------------|
| AT | 0,02 | 0,8 | 10-20 | +++ | da |
| PS | 0,1 | 1 | 5-10 | ++ | ne |
| PC | 0,2 | 1 | 5-10 | ++ | ne |
| FVL homozigot | 0,1 | 3-4 | 60-70 | +++ | da |
| FVL heterozigot | 5-7 | 20-25 | 3-5 | + | da |
| PTM homozigot | 0,01 | - | - | verovatno povišen | da |
| PTM heterozigot | 2 | 6-7 | 3-5 | + | da |
| Hiperhomocisteinemija | 5 | 10-15 | 3 | + | da |
| LA | 1 | 10 | 10 | ++ | da* |
| APA | 2 | 10 | 5 | ++ | da |
| FVIII > 2,3 kIU/L | - | 20 | 5-6 | ++ | da* inflamacija |

LABORATORIJSKA DIJAGNOZA TROMBOFILIIA

ANTITROMBIN - AT (kromogena metoda) (akutna)

Lako snižen AT. Kod urođenog (naslednog) nedostatka nivo je normalno značajno snižen.

Stečen nedostatak se može videti kod tretmana heparinom, DIK-a, oštećenja jetre, maligniteta, nefrotskog sinroma.

Snižen AT koji može odgovarati urođenom (naslednom) nedostatku.

Potvrđen nedostatak (ponovljeno testiranje ili porodično ispitivanje) je udružen sa povećanim rizikom od tromboze.

LABORATORIJSKA DIJAGNOZA TROMBOFILIIA

PROTEIN C - PC (kromogena metoda, antigen ELISA)

PROTEIN S - PS (lateks aglutinacija, antigen ELISA)

Normalan PC, uz snižen slobodni PS. Može se videti kod trudnoće ili terapije estrogenima. Eventualni urođeni (nasledni) nedostatak se ne može utvrditi.

Sniženi PC i PS se mogu videti kod smanjene sinteze u jetri, DIK-a, nedostatka vitamina K, OAT. Za korektno određivanje nedostatka PC ili PS neophodno je da se prekine terapija OAT najmanje dve nedelje pre testiranja.

Snižen PC/PS koji može odgovarati urođenom (naslednom) nedostatku. Potvrđen nedostatak (ponovljeno testiranje ili porodično ispitivanje) je udružen sa povećanim rizikom od tromboze.

LABORATORIJSKA DIJAGNOZA TROMBOFILIIA

LUPUS ANTIKOAGULANS-LA/ANTIFOSFOLIPIDNA ANTITELA-APA

LA (duplicentrifugirana plazma)

DRVVT i senzitivni aPTT (silika)

Jedan pozitivan - potvrda u okviru šest nedelja

APA (ELISA)

Antikardiolipinska i anti beta- 2 glikoprotein 1 antitela

LABORATORIJSKA DIJAGNOZA TROMBOFILIIA

LUPUS ANTIKOAGULANS - LA

LA nije otkriven rutinskom metodom (dRVVT). aPTT je produžen što može da ukaže na prisustvo LA koji se može dokazati aPTT-om ali ne dRVVT.

LA nije otkriven rutinskom metodom (dRVVT). aPTT je produžen. Povišena aktivnost anti-Xa koja ukazuje da je pacijent tretiran heparinom/LMWH tivnost što može biti objašnjenje za produžen aPTT.

LABORATORIJSKA DIJAGNOZA TROMBOFILIIA

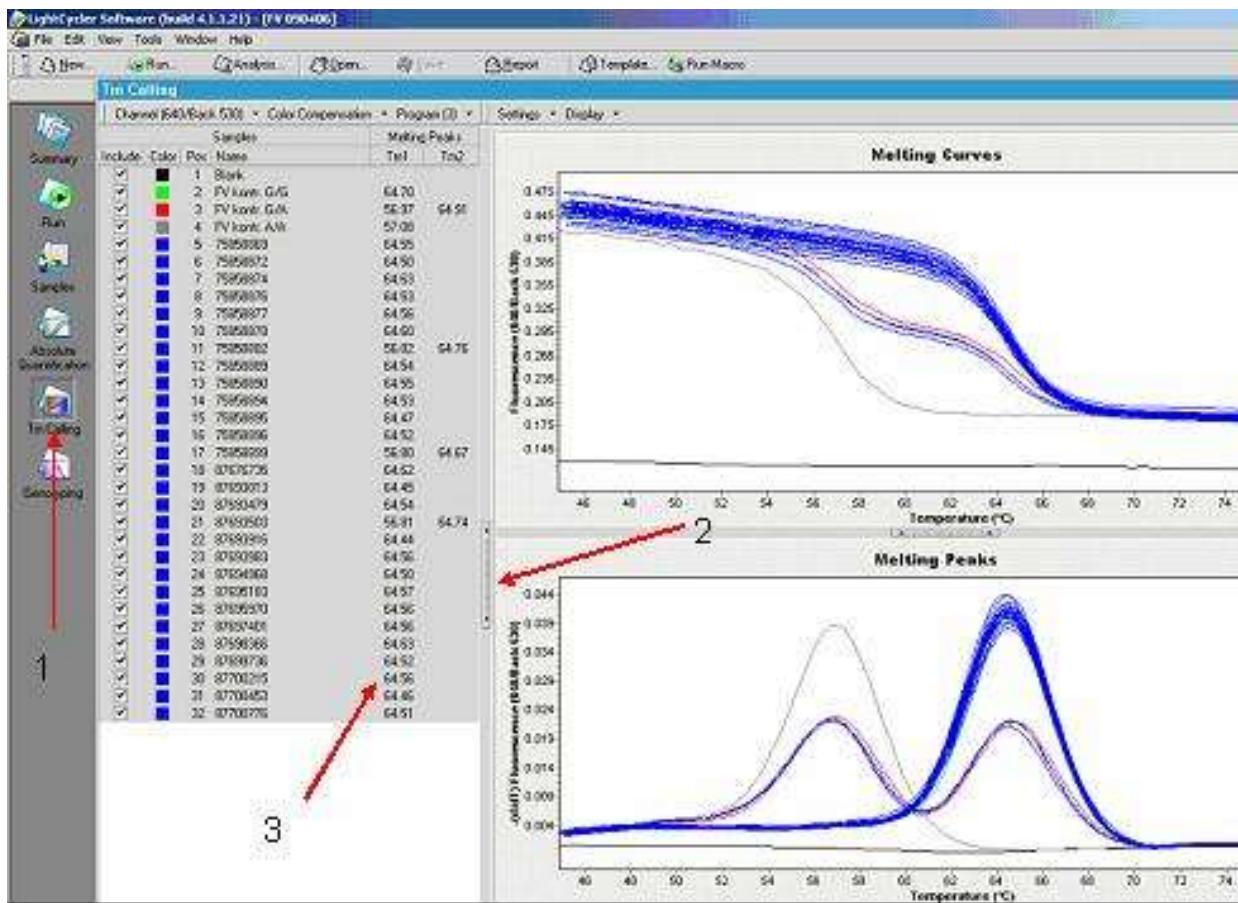
LUPUS ANTIKOAGULANS - LA

LA prisutan. OBS - usled OAT (PK-INR>1,8) mogući lažno pozitivni rezultati.

Prisustvo LA je udruženo sa povećanim rizikom od tromboza kako arterijskih tako i venskih. LA može biti prisutan kod autoimunih bolesti, maligniteta i udružen sa infekcijama.

LABORATORIJSKA DIJAGNOZA TROMBOFILIIJA

PCR – Light cycler FVL/PTM



LABORATORIJSKA DIJAGNOZA TROMBOFILIIA

Faktor VIII (FVIII)

Povišen nivo FVIII može biti prisutan u trudnoći ili usled inflamacije. Kod visokih vrednosti ($>2,3$) je povećan rizik od tromboza).

LABORATORIJSKA DIJAGNOZA TROMBOFILIIJA

ARTERIJSKE TROMBOZE - PAI-1/Lp(a)

Lako do umereno povišen nivo PAI-1 (16-30). U kombinaciji sa drugim faktorima rizika (lipidi, gojaznost) može biti faktor rizika za kardiovaskularne bolesti.

Jako povišen nivo PAI-1 (>30), ukazuje na snižen fibrinolitički kapacitet i od značaja je za trombozu. (PAI-1 je protein akutne faze i povičen je kod zapaljenja).

Povišen nivo PAI-1 javlja se udružen sa poremećajem lipida, gojaznošću i smanjenom fizičkom aktivnošću (metabolički sindrom).

Povišen nivo Lp(a) iznad 0,3 g/L je udružen sa 2-3 puta većim rizikom od kardio- i cerebro-vaskularnih oboljenja.

ANTIKOAGULATNI LEKOVI

- ☒ HEPARIN
- ☒ LMWH
- ☒ DIREKTNI TROMBIN INHIBITORI
- ☒ DIREKTNI XA INHIBITORI
- ☒ PENTASAHARIDI
- ☒ ORALNA ANTIKOAGULANTNA TERAPIJA (WARFARIN)

Nepoznat/neotkriven uzrok

| | Dužina terapije |
|--|-------------------------|
| Prva distalna DVT (ispod v poplitea-e) privremen faktor rizika | 6 nedelja |
| Prva distalna DVT nepoznat/stalan faktor rizika proksimalna prva embolija pluća | 6 meseci |
| Ako je povećan rizik od krvarenja | 3 meseca |
| Prva DVT/PE životno ugrožavajuća | 12 meseci |
| Prva DVT/PE aktivni kancer | Do izlečenja kancera |
| Druga DVT kontralateralna | Kao prva |
| Druga DVT Ipsilateralna PE | >12 meseci |
| Tri ili više | Do dalnjeg |

Tromboza i trombofilije

| | Dužina terapije |
|------------------------------------|--------------------------|
| AT | Do dalnjeg |
| Homozigoti ¹ | Do dalnjeg |
| Dvostruki heterozigoti | Do dalnjeg |
| Životno ugrožavajuća uz deficit | Do dalnjeg |
| PC ili PS | >12 meseci |
| LA/AKA | Više godina ² |
| FVIII >2,3 IE/mL | >6 meseci |
| Hiperhomocisteinemija ³ | Kao bez trombofilije |
| FVL/PTM heterozigot | Kao bez trombofilije |

¹Mogući izuzetak PTM

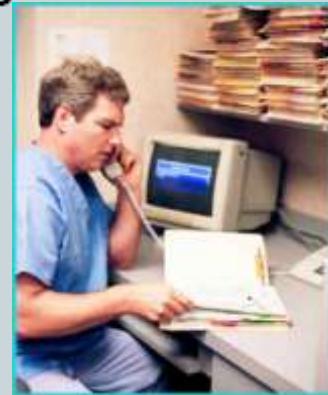
² Dva uzastopna negativna nalaza – razlog za prekid

³ Vitamin B

GLOBALNI HEMOSTATSKI METODI

...capable of assessing hemostatic potential, and predicting clinical outcomes: bleeding or thrombosis

- “Ideally the clinician requires a single laboratory test that correlates with the overall risk of a patient. This test is currently not available....
- “One can perhaps envisage that as we have simple global tests of hypocoagulability such as the PT and APTT, it may soon become possible to measure multi-factorial thrombophilia without resorting to the multiple tests currently necessary.”



(Mannucci, PM. Thromb. Haemost. 2002)

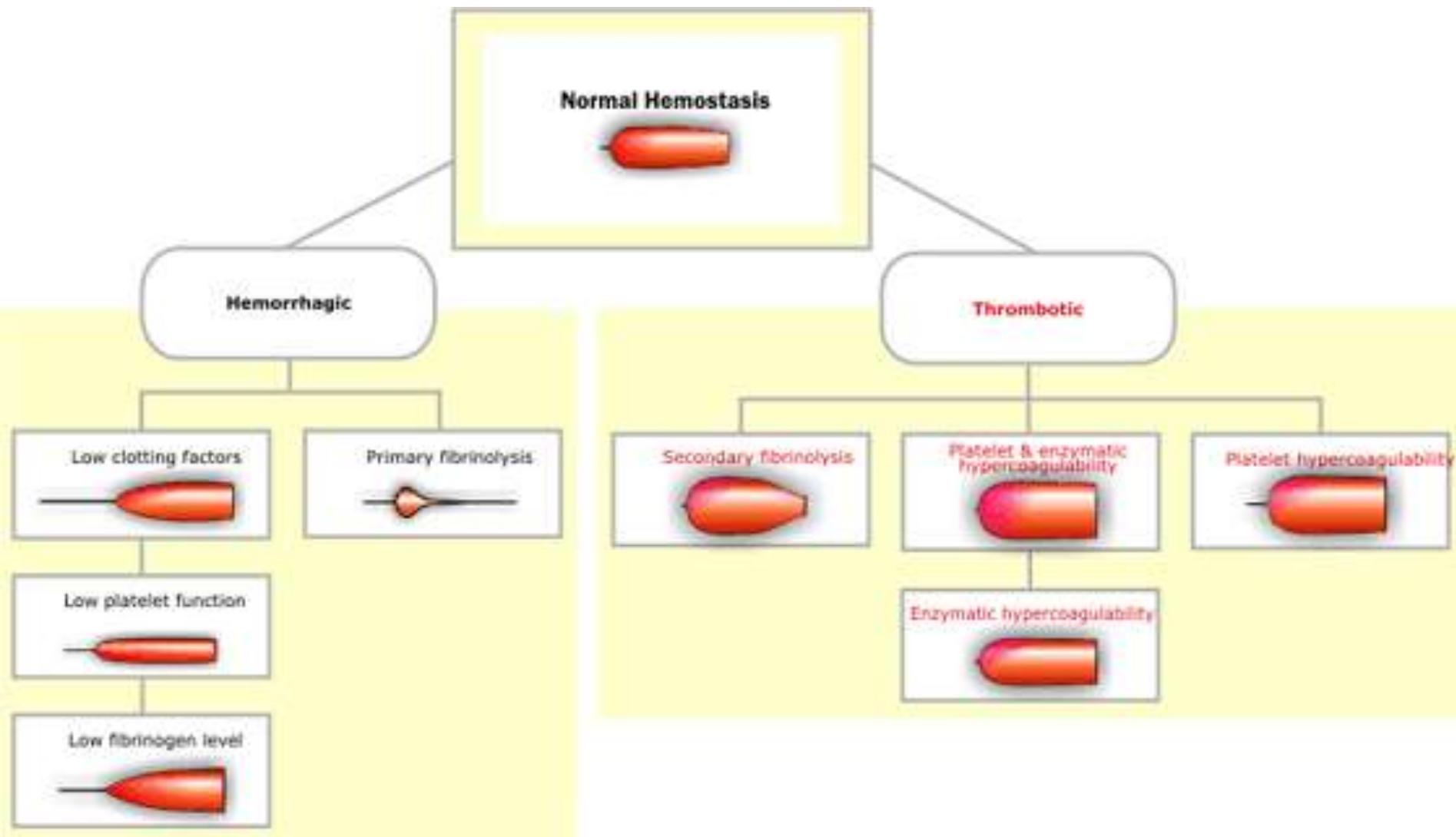
Modifikovani APTT - "transmitance waveform" (TW)

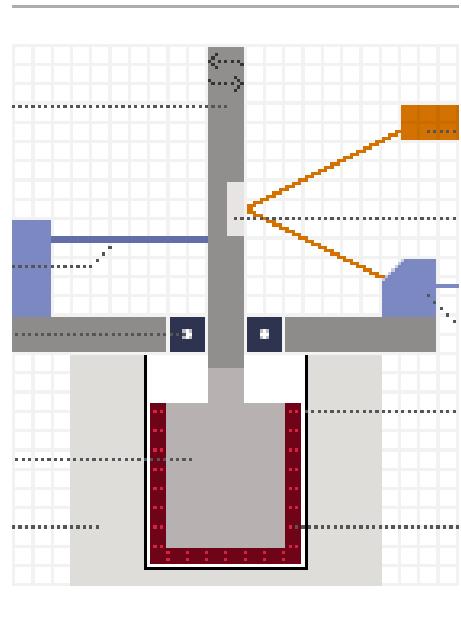
Endogeni trombin potencijal (ETP)

Tromboelastografija (TEG)/ROTEG

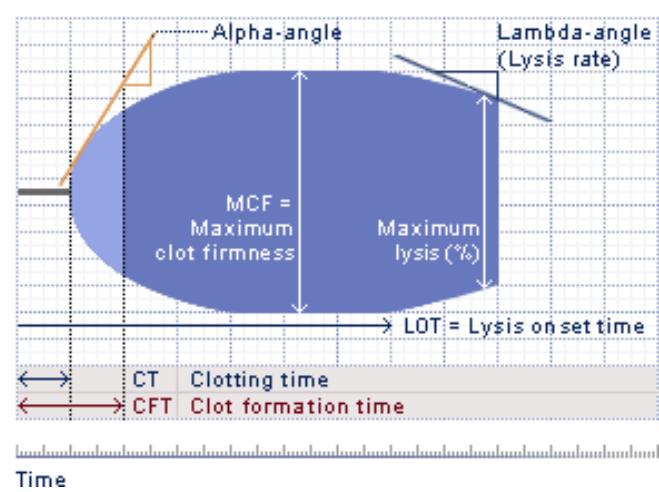
Ukupni hemostatski potencijal (OHP)

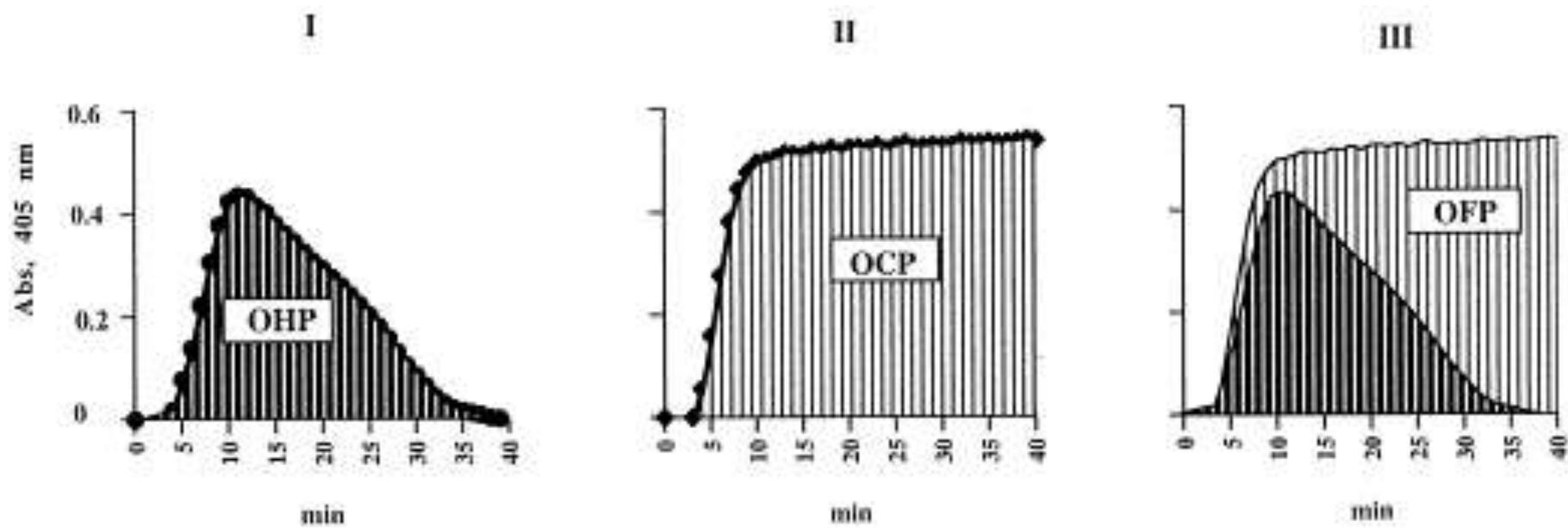


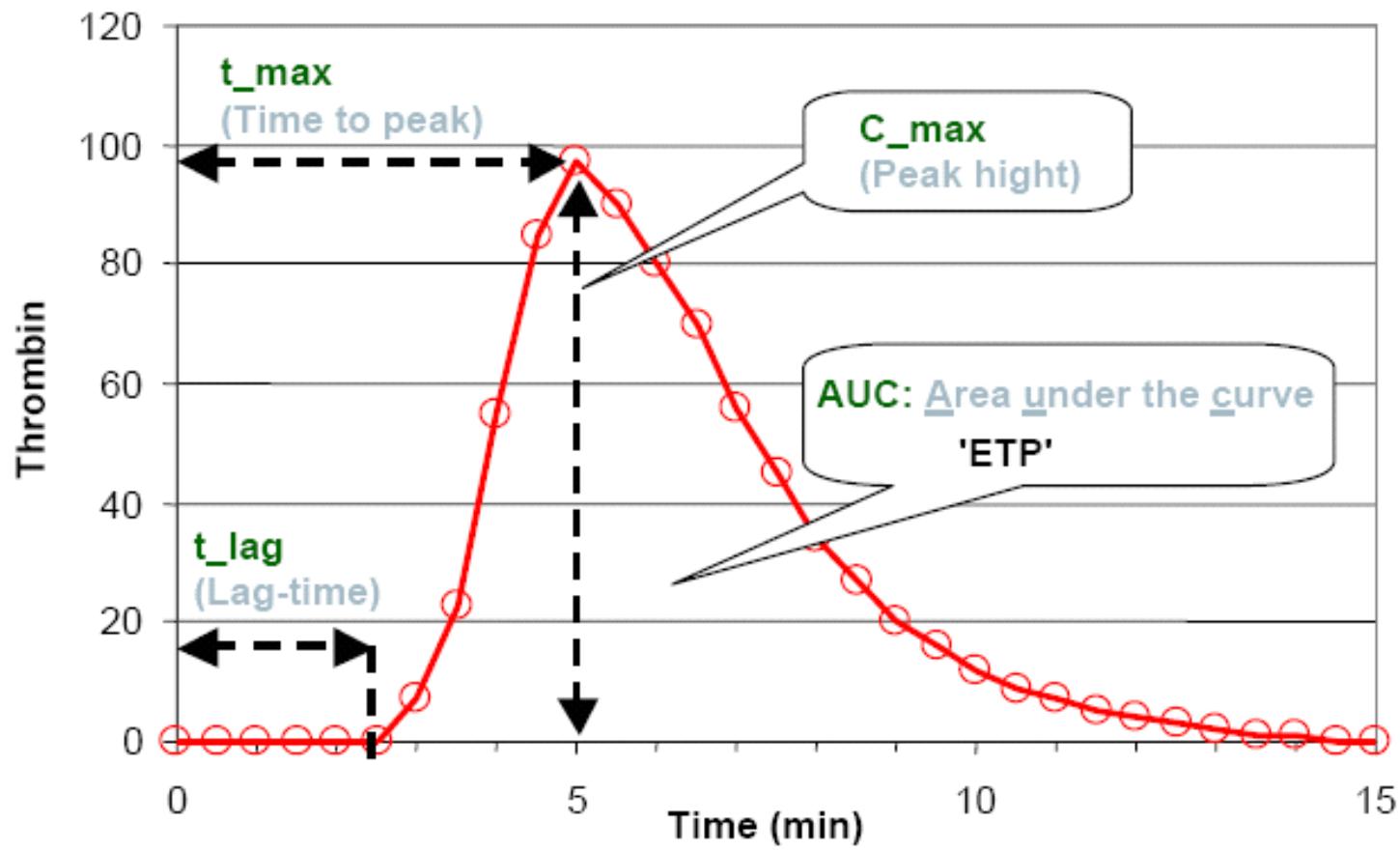




Parameters of ROTEG® Analysis







Lawrie A, Béguin S, Hemker H C, Henckel T, Samama M, Woodhams B, Gray E. (2005)
 The Thrombin Generation Test (TGT); On behalf of the International Society on Thrombosis and Haemostasis (ISTH) Scientific and Standardization Committee (SSC) Working Group on Thrombin Generation Tests. www.blood.com, 2005.

UMESTO ZAKLJUČAKA

- Izbor pacijenata, testova i vremena testiranja
- Centralizovana dijagnostika
- Interna i eksterna kontrola
- Tumačenje rezultata
- Značaj za pacijenta i rođinu

MESSAGE TO TAKE HOME

Uvek imati na umu zašto testiramo

Laboratorija je samo pomoć ne osnova dijagnoze

DIJAGNOSTIKA TROMBOFILIIJA NIJE AKUTNA DIJAGNOSTIKA

Akutni testovi u hemostazi su:

PT, aPTT, Fibrinogen, AT, FVIII, D-dimer

