TEKRARLAYAN GEBELİK KAYIPLARI

PROF.DR.SEDAT KADANALI

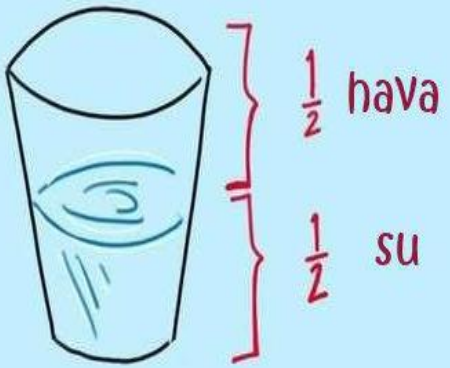
Definitions of infertility and recurrent pregnancy loss: a committee opinion

Practice Committee of the American Society for Reproductive Medicine

Recurrent pregnancy loss is a disease* distinct from infertility, defined by two or more failed pregnancies. When the cause is unknown, each pregnancy loss merits careful review to determine whether specific evaluation may be appropriate.

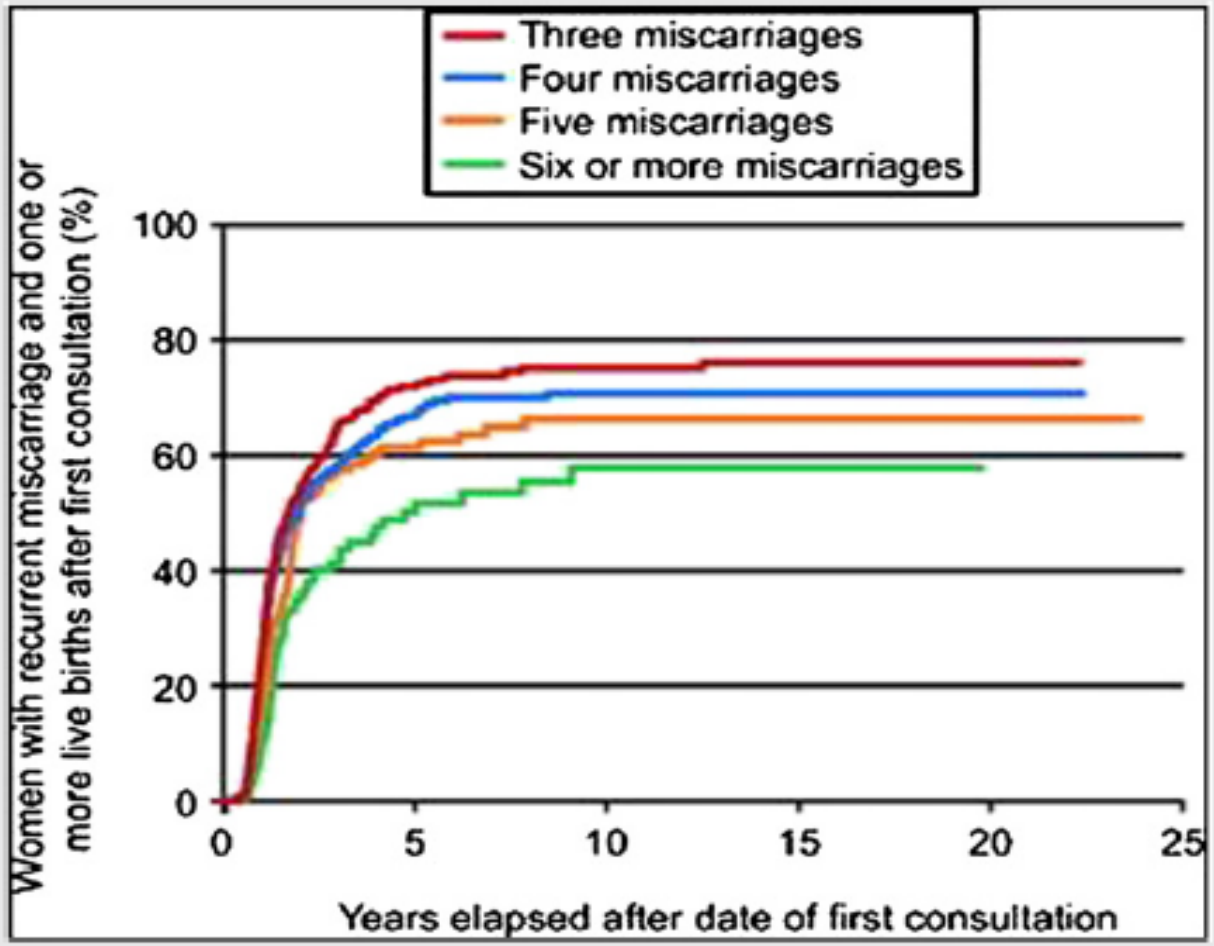
TGK Riski

Outcome	Prior Losses	Recurrence Risk %
Liveborn	0	12
	1	24
	2	26
	3	32
	4	26
No Live Births	1	19
	2	35
	3	47
	4	54



teknik olarak, bardagın tamamı dolu.

FIGURE 1



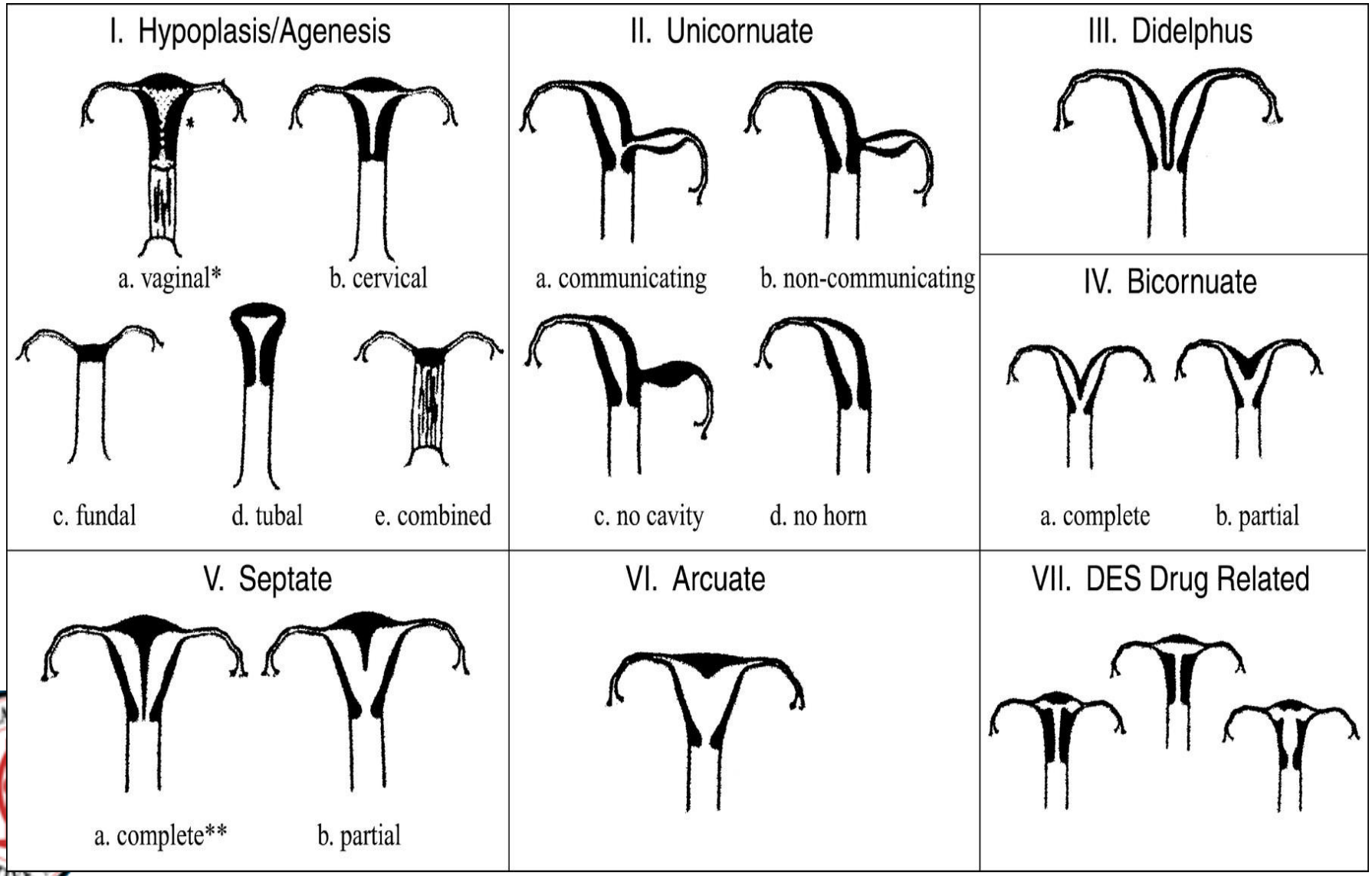
Kaplan-Meier plot showing percentage of women in the recurrent miscarriage cohort who have had at least one live birth after first consultation by number of miscarriages before first consultation. (Lund et al. Recurrent miscarriage and prognosis for live birth. Obstet Gynecol 2012.)

Practice Committee. Recurrent pregnancy loss. Fertil Steril 2012.

ETYOLOJİK FAKTÖRLER

- Anatomik Faktörler %12-16
- Genetik Faktörler %3.5-5
- Endokrin Faktörler %17-20
- İnfeksiyöz Faktörler %0.5-5
- İmmünolojik Faktörler %20-50
- Diğer Faktörler %10

Classification system of Mullerian duct anomalies developed by the American Fertility Society



İnfeksiyon

- TGK ile hiçbir enfeksiyöz ajanın ilişkisi gösterilememiştir.
  - *Ureaplasma urealyticum , Mycoplasma huminis, chlamidya, Listeria monocytogenesis, Toxoplasma gondii, rubella, HSV, CMV*, etc
  - Bu organizmaların TGK de rutin taranması gereksizdir.
  - Antibiyotik kullanımı da gereksizdir.

Thrombophilia

- En sık kalıtımsal olanlar
  - Heterozygous Factor V Leiden (G1691A)
  - Factor II-prothrombin mutation (G20210A)
  - Hyperhomocysteinemia (MTHFR C677T and A1298C)
- Diğer muhtemel anomaliler
  - Anti-thrombin eksikliği
  - Protein C or S eksikliği
  - Factor VIII Artışı

Ülkemizde TGK-Trombofili çalışmaları

ARAŞTIRICI	TGK N:	KONTROL N:	MTHFR FV LEİDEN PRT G	SONUÇ
Şahin İF, ark	205	100	+	ANLAMSIZ
Altıntaş A. ve ark	114	185	+	ANLAMSIZ
Özdemir S ve ark.	251	50	+	ANLAMSIZ
Gazi Y. ve ark	57	47	+	ANLAMSIZ
Eminov E.	166	74	+	ANLAMSIZ
İmir G ve ark.	272	52	+	ANLAMLI

Thrombosis Research (2009) 123 Suppl. 2, S105–S110

THROMBOSIS RESEARCH

intl.elsevierhealth.com/journals/thre

Thrombophilia and pregnancy loss: cause or association

Jean-Christophe Gris*

Department of Haematology, University Hospital, Nîmes; Faculty of Pharmacy and research team EA 2992, University of Montpellier, France

The natura

P. G. LINDQVIST
Departments of Obstetr *sity, Malmö, Sweden*

To cite this article: Lind *6–7.*

See also Lindqvist PG, M *Haemost* 2005; 3: 221–3; Brenner B, Ho *f enoxaparin in* women with thromboph

The wom
pregnanc
coagulat
advance
until at l

suring
own in
zed

Table 1 Pregnancy outcome in different subgroups of women with prior fetal loss

	Prior live birth rate (%)	Present live birth rate (%)
Recurrent fetal loss		
Enoxaparin 40 or 80 mg ($n = 50$) [3]*	20	75
Enoxaparin 40 mg ($n = 89$) [4]*	28	84
Enoxaparin 80 mg ($n = 91$) [4]*	28	78
No treatment ($n = 37$)†,**	28	89
Second trimester fetal loss		
1 prior ($n = 43$) no treatment**	49	98
≥2 prior ($n = 10$) prior no treatment**	30	80
Nulliparous women with one prior fetal losses and carriers of factor V Leiden (FVL)		
Low-dose Asprin ($n = 36$) [7]	0	29
Enoxaparin 40 mg ($n = 36$) [7]	0	94
No treatment ($n = 20$)‡,**	0	95
No treatment ($n = 52$)§,**	40	98

Recurrent fetal loss ≥3 first trimester and/or ≥2 second trimester fetal loss.
*Includes or/and ≥1 stillbirth.
†Includes women with and without thrombophilia.
‡Nulliparous carriers of FVL with at least 1 prior fetal loss.
§FVL carriers with at least 1 prior fetal loss.
**Present study.

Kalıtımsal trombofililer ile TGK arasında ilişki olabileceği iddia edilmişse de çalışmalarda bu doğrulanmamıştır.

Evaluation and treatment of recurrent pregnancy loss: a committee opinion

The Practice Committee of the American Society for Reproductive Medicine

American Society for Reproductive Medicine, Birmingham, Alabama

TGK lı kadınlar kalıtımsal trombofililer açısından rutin olarak incelenmemelidir.

The major
pregnancy
cases of RI
American
Earn onlir

Discuss: You can discuss this article with its authors and with other ASRM members at http://fertstertforum.com/goldsteinj-evaluation-treatment-recurrent-pregnancy-loss-committee-opinion/

* Download a free QR code scanner by searching for "QR scanner" in your smartphone's app store or app marketplace.

enetics
Medicine

ACM

THFR

Scott E. Hic

D, FACMG[3]

BOX 1: ACMG RECOMMENDATIONS

- *MTHFR* polymorphism genotyping should not be ordered as part of the clinical evaluation for thrombophilia or recurrent pregnancy loss
- *MTHFR* polymorphism genotyping should not be ordered for at-risk family members
- A clinical geneticist who serves as a consultant for a patient in whom an *MTHFR* polymorphism(s) is found should ensure that the patient has received a thorough and appropriate evaluation for his or her symptoms
- If the patient is homozygous for the "thermolabile" variant c.665C→T, the geneticist may order a fasting total plasma homocysteine, if not previously ordered, to provide more accurate counseling
- *MTHFR* status does not change the recommendation that women of childbearing age should take the standard dose of folic acid supplementation to reduce the risk of neural tube defects as per the general population guidelines[71–77]

APS Kriterleri

- Laboratuar bulguları
- Anti-cardiolipin (aCL) antikorlar: IgG veya IgM, 2 kez veya daha fazla, en az 12 hafta aralıklarla orta veya üst derece yüksek seviyelerinin ölçümü
- Lupus anticoagulant (LA) antikorlar: 2 kez veya daha fazla, en az 12 hafta aralıklarla
- Anti-β2 glycoprotein I (IgG or M) 2 kez veya daha fazla, en az 12 hafta aralıklarla

RECURRENT PREGNANCY LOSS

TABLE 2

Prevalence of abnormal results for each evidence-based diagnostic test from 1020 patients with RPL.

Test	No. of consecutive pregnancy losses				Total (n = 1020)	Control populations
	2 (n = 447)	3 (n = 343)	≥4 (n = 230)	*P* value		
Parental genetics	2.8 (8/281)	5.4 (15/280)	5.2 (11/212)	.28	4.4 (34/773)	0.4 (4/1000)[a]
Uterine anatomy	18.7 (75/401)	18.2 (55/303)	16.7 (34/203)	.84	18.1 (164/907)	7.5 (148/1961)[b]
Lupus anticoagulant	5.0 (20/400)	2.9 (9/307)	1.9 (4/216)	.10	3.6 (33/923)	[c]
Anticardiolipin	15.6 (64/409)	13.1 (42/320)	17.1 (37/217)	.42	15.1 (143/946)	6.7 (7/104)[d]
Factor V Leiden	4.2 (6/144)	8.1 (8/99)	10.3 (7/68)	.21	6.8 (21/311)	6.8 (25/366)[e]
TSH	8.1 (32/396)	6.5 (19/291)	6.2 (12/194)	.62	7.2 (63/881)	3.9 (241/6182)[f]
Blood glucose	0 (0/193)	0.8 (1/124)	0 (0/73)	.34	0.3 (1/390)	[g]

TABLE 4

Prevalence of abnormal results for each investigative diagnostic test given to 1018[a] patients with RPL.

Test	No. of consecutive pregnancy losses: 2	3	≥4	*P* value	Total	Control populations
Antiphosphatidyl serine antibodies[b]	4.6 (18/391)	5.6 (16/288)	7.8 (15/193)	.29	5.6 (49/872)	0.5 (2/392)[c]
Microbial infection	16.5 (70/425)	13.6 (45/331)	16.2 (37/228)	.52	15.4 (152/984)	20.0 (27/135)[d]
Midluteal P	16.7 (63/377)	16.7 (47/281)	16.1 (31/193)	.98	16.6 (141/851)	9.4 (5/53)[e]
PRL	5.9 (21/358)	6.1 (16/264)	4.8 (9/186)	.84	5.7 (46/808)	0.4 (40/10,000)[f]
Functional protein C activity	0.9 (1/115)	0 (0/85)	3.3 (2/61)	.17	1.1 (3/261)	2.0 (7/345)[g]
Functional protein S activity	3.5 (4/115)	2.4 (2/85)	5.0 (3/60)	.69	3.5 (9/260)	3.5 (9/254)[g]
Antithrombin activity	2.6 (3/115)	0 (0/85)	1.6 (1/61)	.33	1.5 (4/261)	0.8 (2/264)[g]
Homocysteine/ MTHFR	15.1 (22/146)	10.2 (10/98)	17.1 (12/70)	.39	14.0 (44/314)	5.2 (13/249)[h]
Factor II mutation	2.7 (2/74)	4.8 (2/42)	3.7 (1/27)	.84	3.5 (5/143)	1.7 (6/359)[g]

Table II. Recommendation for the testing of couple presenting with recurrent miscarriage (≥3 miscarriages)

Basic investigations

Obstetric and family history, age, BMI, organic solvents, alcohol, mercury, lead, caffeine, hyperthermia, smoking

- Full blood count (blood sugar level and thyroid function tests)
- Antiphospholipid antibodies (LAC and aLC)
- Parental karyotype (after 2 miscarriages—see Table I)
- Pelvic ultrasound (SIS) and/or hysterosalpingogram and hysteroscopy and laparoscopy in case of inconclusive findings

Research investigations within the context of a trial

- Feto-placental karyotypes
- Testing of uterine and/or peripheral blood NK cells
- Mannan-binding lectin (MBL) level
- Luteal phase endometrial biopsy
- Homocysteine/folic acid level
- Thrombophilia screening

Table III. Recommendation for the medical treatment of women with recurrent miscarriage (RM) (≥3 consecutive miscarriages)

Established treatment

- Tender loving care (TLC) and health advices (diet, coffee, smoking and alcohol)

Treatment requiring more RCTS

- Aspirin and/or LMW heparins for women presenting with APS or (multiple) inherited thrombophilias
- Progesterone in women presenting with unexplained early and late RM
- IVIG in women presenting with unexplained secondary RM or late RM
- Folic acid in women presenting with hyperhomocysteinaemia
- Immunization with third-party donor leukocyte

Treatment of no proven benefit

- Immunization with paternal leukocytes or trophoblast membranes
- Multivitamins supplementation

Treatment associated with more harm than benefit

- Daily corticoids during the first half of pregnancy

Evaluation and treatment of recurrent pregnancy loss: a committee opinion

The Practice Committee of the American Society for Reproductive Medicine

American Society for Reproductive Medicine, Birmingham, Alabama

The majority of miscarriages are sporadic and most result from genetic causes that are greatly influenced by maternal age. Recurrent pregnancy loss (RPL) is defined by two or more failed clinical pregnancies, and up to 50% of cases of RPL will not have a clearly defined etiology. (Fertil Steril® 2012;98:1103–11. ©2012 by American Society for Reproductive Medicine.)

November 2012

TABLE 1

Suspected causes of recurrent pregnancy loss.

Cause	Contribution to RPL (%)	Recommended screening	Supportive scientific evidence	Controversial scientific evidence	Not recommended
Cytogenetic	2–5	Balanced reciprocal translocations			
aPL syndrome	8–42 (mean, 15)	Lupus anticoagulant, anticardiolipin IgG or IgM antibody, anti-β_2-glycoprotein I	IgG and IgM antibodies, aPL testing for other phospholipids and β_2 glycoprotein I	IgG or IgM anti-annexin A5, anti-factor XII, anti-prothrombin, IgA aPLs	ANA, antithyroid antibodies
Anatomic	1.8–37.6 (mean, 12.6)	Hysterosalpingography Sonohysterography	Congenital uterine abnormalities	Uterine fibroids, polyps	Cervical incompetence
Hormonal or metabolic		Prolactin TSH Hemoglobin A1c	Uncontrolled diabetes or thyroid disease, prolactin	Polycystic ovary syndrome and insulin resistance, luteal phase progesterone	
Infectious		None		Bacterial vaginosis, endocervical infections	
Male factors		None		Abnormal sperm DNA	
Psychological		None		Psychological effects on uterine receptivity	
Alloimmune		None		Mucosal CD16– NK cells, embryotoxic factor, cytokine profiles, blocking antibodies, HLA typing, anti-paternal leukocyte antibodies, circulating CD16– NK cells	Circulating CD16– NK cells
Environmental, occupational, or personal habits		History			Not related to recurrent pregnancy loss

Note: ANA = antinuclear antibodies; aPL = antiphospholipid.

Practice Committee. Recurrent pregnancy loss. Fertil Steril 2012.

TGK Araştırılması

- Ararda 2 kayıptan sonra araştırılmalıdır
- Eşlerin karyotipisi
- aCL, LA ve Anti-β2 glycoprotein I
- Sonohysterogram, hysterosalpingogram and /or Hysterescopy
- Troid or prolaktin anormallikleri ve kontrolsüz diabet

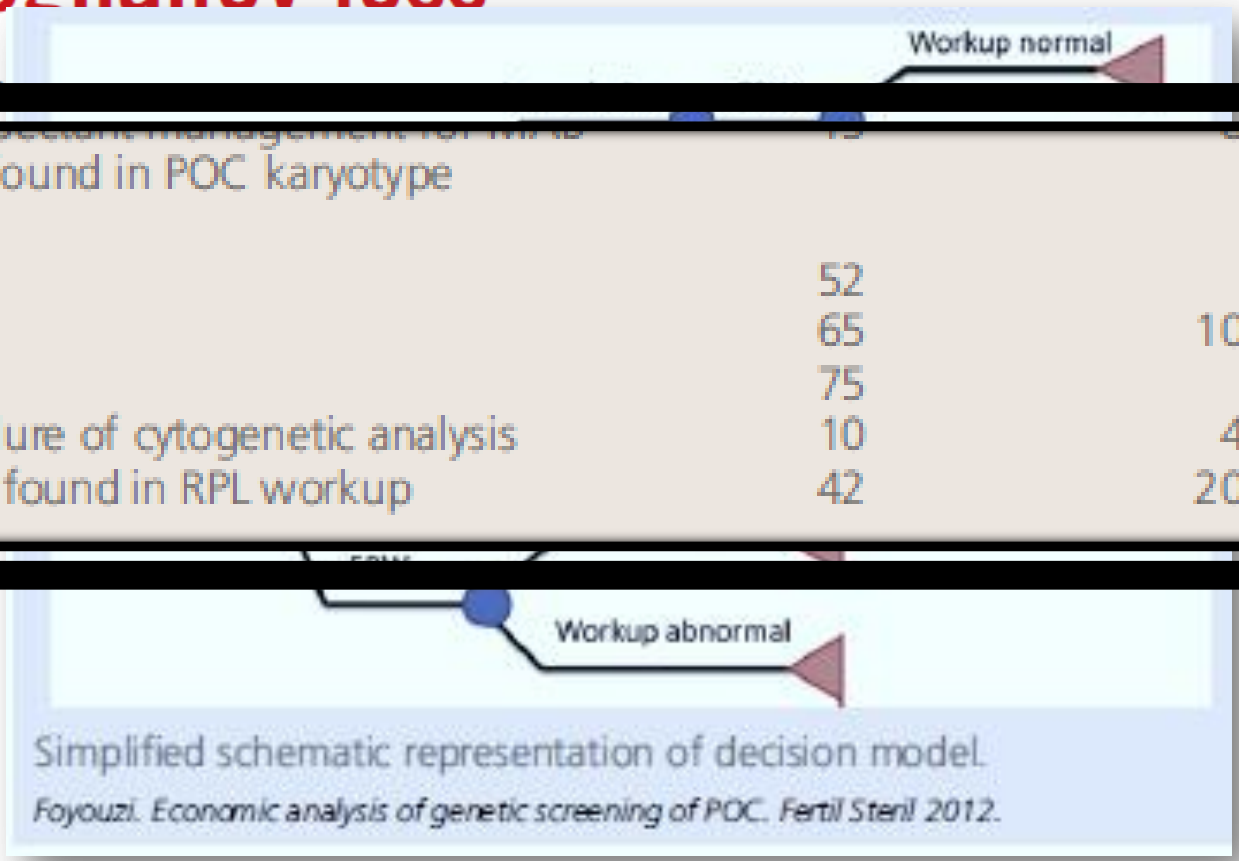
TGK de önerilmeyen testler

- İnfeksiyon
- ANA, anti-troit antikorlar
- Trombofili taraması
- CD 16, CD 56, NK hücrelere bakılması
- Blokan antikorlar, HLA tiplemesi
- Sperm DNA fragmantasyonu

	Adet	Doktor Adı	Toplam	Kurum	Hasta
LABORATUVAR HİZMETLERİ	**22**		**3,000.00**	**0.00**	**3,000.00**
ANA (Anti Nükleer Antikoru)	*1*		*63.66*	*0.00*	*63.66*
Anti-Beta-2 Glikoprotein I IgG	*1*		*71.62*	*0.00*	*71.62*
Anti-Beta-2 Glikoprotein I IgM	*1*		*71.62*	*0.00*	*71.62*
Anti-Kardiyolipin IgG antikoru(ACA IgG)	*1*		*66.05*	*0.00*	*66.05*
Anti-Kardiyolipin IgM antikoru(ACA IgM)	*1*		*66.05*	*0.00*	*66.05*
Anti-Trombin III	*1*		*67.64*	*0.00*	*67.64*
APTT (Akt. Pars. Tromboplastin zaman)	*1*		*26.26*	*0.00*	*26.26*
CD19	*1*		*52.52*	*0.00*	*52.52*
CD3 Total T Lenfosit	*1*		*52.52*	*0.00*	*52.52*
CD4 T-Helper Lenfosit	*1*		*55.70*	*0.00*	*55.70*
CD56	*1*		*52.52*	*0.00*	*52.52*
CD8 T-Supressor Lenfosit	*1*		*54.91*	*0.00*	*54.91*
HLA doku tiplendirmesi (A,B,C,DR)	*1*		*795.75*	*0.00*	*795.75*
Homosistein (serum)	*1*		*77.19*	*0.00*	*77.19*
Interleukin 1 Alfa	*1*		*266.58*	*0.00*	*266.58*
Interleukin 6 Alfa	*1*		*266.58*	*0.00*	*266.58*
Interleukin 8 Alfa	*1*		*298.41*	*0.00*	*298.41*
Lupus antikoagulanları	*1*		*79.58*	*0.00*	*79.58*
PRA (Panel Reactive Antikor)	*1*		*318.30*	*0.00*	*318.30*
Protein C Aktivitesi	*1*		*89.12*	*0.00*	*89.12*
Protein S Aktivitesi	*1*		*89.12*	*0.00*	*89.12*
PT (Protrombin zamanı)	*1*		*18.30*	*0.00*	*18.30*
		Genel Toplam	**3,000.00**	**0.00**	**3,000.00**

Cost-effectiveness of cytogenetic evaluation of products of conception in the patient with a second pregnancy loss

Aneuploidy found in POC karyotype		
<35	52	
35–40[a]	65	10–80
>40	75	
Technical failure of cytogenetic analysis	10	4–16
Abnormality found in RPL workup	42	20–80



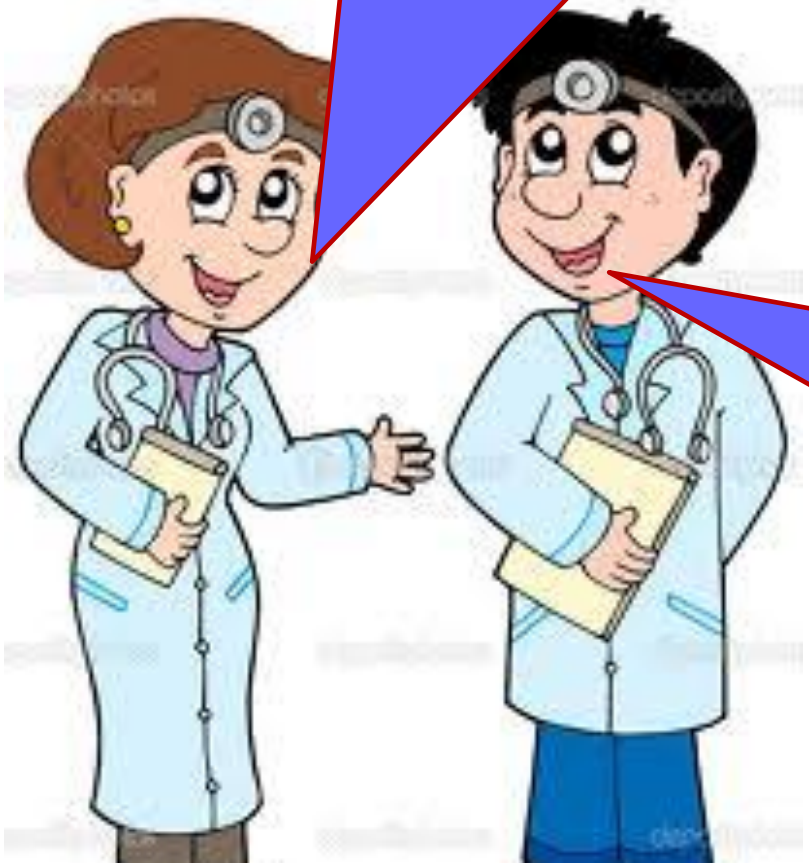
Simplified schematic representation of decision model.

Foyouzi. Economic analysis of genetic screening of POC. Fertil Steril 2012.

Açıklanamayan RPL de antitrombotik tedavi

	N	Ajan da Abort %	Karşılaştırılan Abort %	Rölatif Risk(RR)	SONUÇ

Açıklanamayan düşüklerde antitrombotik tedavinin faydası olmadığı gösterildi. Ben kullanmıyorum

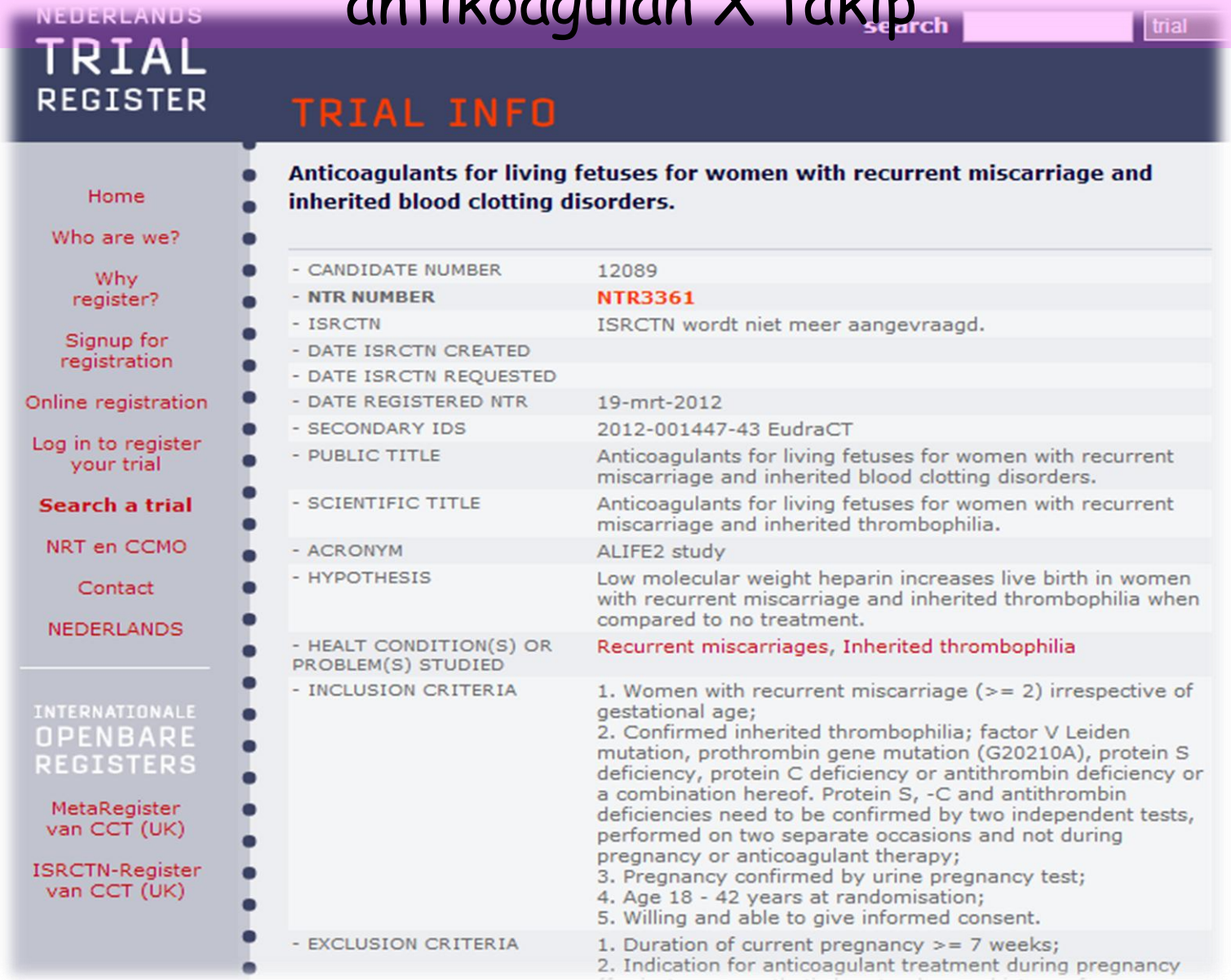


Sen çalışmaları iyi okumamışsın

Most of the women included in these **two pragmatic trials did have good spontaneous prognoses** and recovery rates (regulatory early events due to the repetitionof the sporadic loss risk, mainly favoured by abnormal embryonic karyotypes).
The obtained negative results were expected since the **included women were the worst candidates** for such trials

The authors of these two indubitably planned-to-be-negative trials must be congratulated: they are going **to contribute to sanitize the widespread use of LMWH** in non-selected women with nonclinically categorised pregnancy losses.

ALİFE2: Trombofilisi olan gebelerde antikoagulan X takip



NEDERLANDS TRIAL REGISTER

search trial

TRIAL INFO

Home
Who are we?
Why register?
Signup for registration
Online registration
Log in to register your trial
Search a trial
NRT en CCMO
Contact
NEDERLANDS

INTERNATIONALE OPENBARE REGISTERS
MetaRegister van CCT (UK)
ISRCTN-Register van CCT (UK)

Anticoagulants for living fetuses for women with recurrent miscarriage and inherited blood clotting disorders.

- CANDIDATE NUMBER	12089
- **NTR NUMBER**	**NTR3361**
- ISRCTN	ISRCTN wordt niet meer aangevraagd.
- DATE ISRCTN CREATED	
- DATE ISRCTN REQUESTED	
- DATE REGISTERED NTR	19-mrt-2012
- SECONDARY IDS	2012-001447-43 EudraCT
- PUBLIC TITLE	Anticoagulants for living fetuses for women with recurrent miscarriage and inherited blood clotting disorders.
- SCIENTIFIC TITLE	Anticoagulants for living fetuses for women with recurrent miscarriage and inherited thrombophilia.
- ACRONYM	ALIFE2 study
- HYPOTHESIS	Low molecular weight heparin increases live birth in women with recurrent miscarriage and inherited thrombophilia when compared to no treatment.
- HEALT CONDITION(S) OR PROBLEM(S) STUDIED	Recurrent miscarriages, Inherited thrombophilia
- INCLUSION CRITERIA	1. Women with recurrent miscarriage (>= 2) irrespective of gestational age; 2. Confirmed inherited thrombophilia; factor V Leiden mutation, prothrombin gene mutation (G20210A), protein S deficiency, protein C deficiency or antithrombin deficiency or a combination hereof. Protein S, -C and antithrombin deficiencies need to be confirmed by two independent tests, performed on two separate occasions and not during pregnancy or anticoagulant therapy; 3. Pregnancy confirmed by urine pregnancy test; 4. Age 18 - 42 years at randomisation; 5. Willing and able to give informed consent.
- EXCLUSION CRITERIA	1. Duration of current pregnancy >= 7 weeks; 2. Indication for anticoagulant treatment during pregnancy

Açıklanamayan RPL de antitrombotik tedavi

RCOG 2011

supportive care (Grade B)
NO recommendation for or against treatment

ACCP 2012

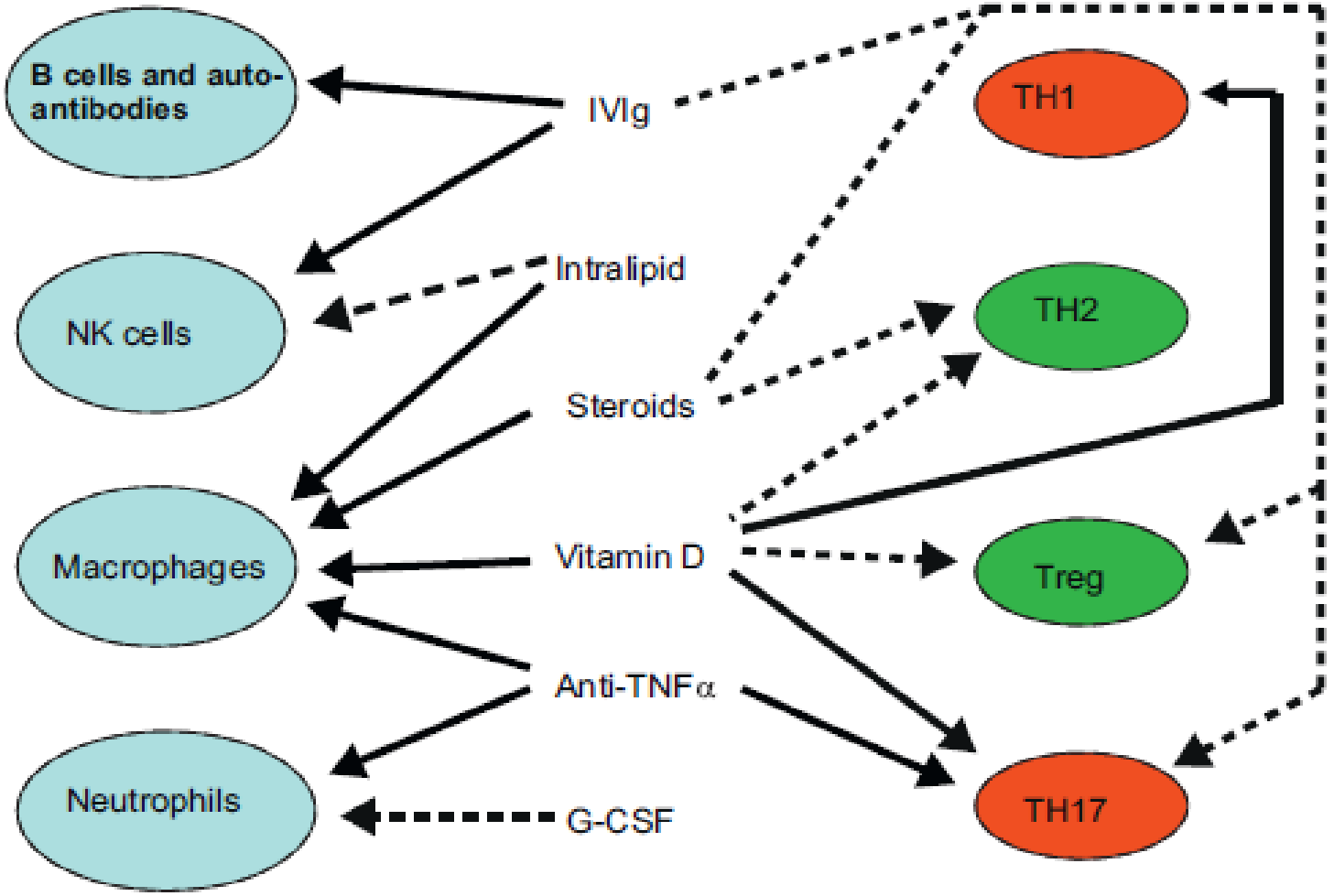
recommend AGAINIST antithrombotic prophylaxis (Grade 1B)

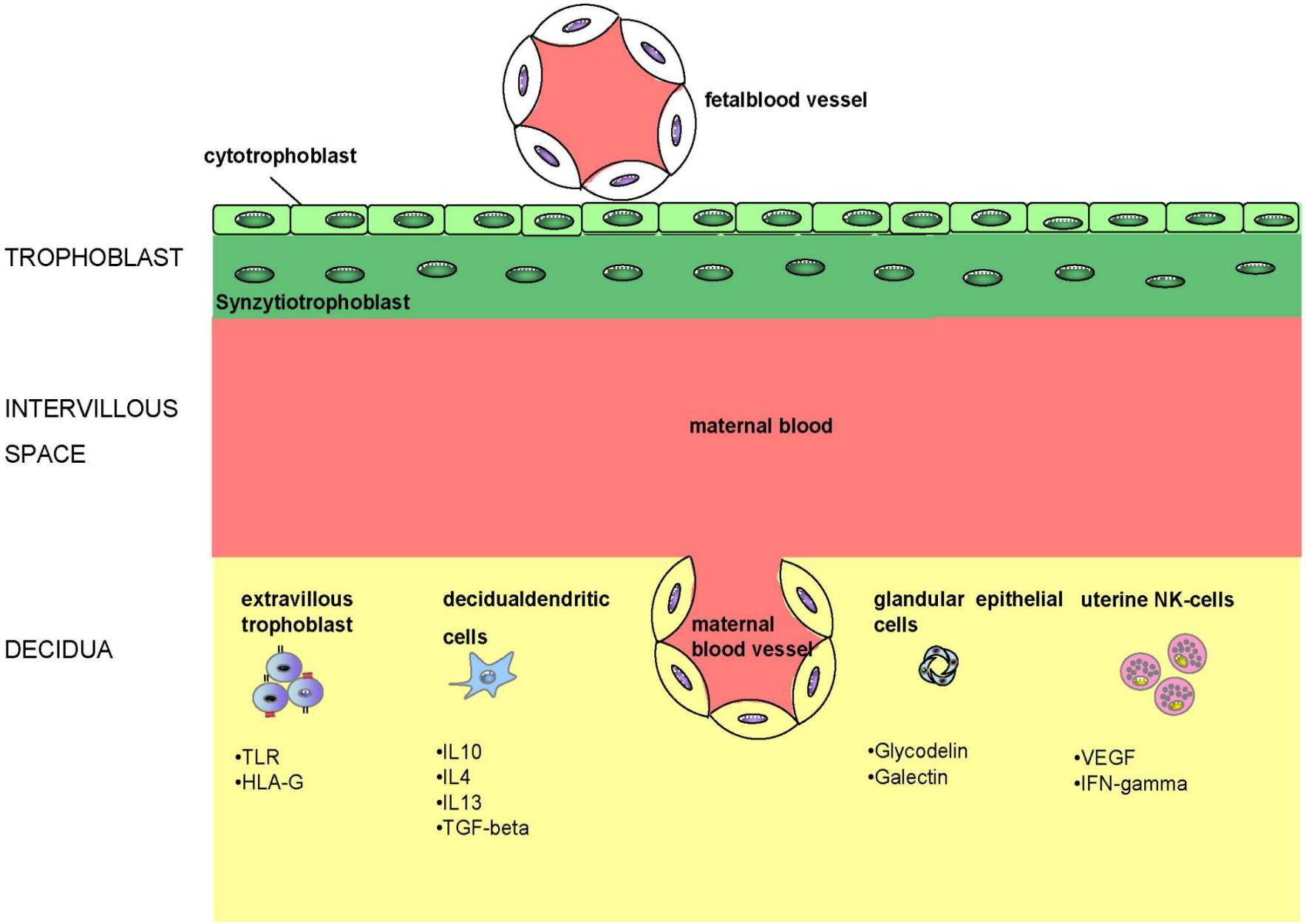
SIGEP/ ESHRE-2006

limited to recommend their routine use

TGK da İmmunomodulatuar Tedaviler

A.S. Bansal et al. / Journal of Reproductive Immunology 93 (2012) 41–51




fetalblood vessel
cytotrophoblast
TROPHOBLAST
Synzytiotrophoblast
INTERVILLOUS SPACE
maternal blood
DECIDUA
extravillous trophoblast
•TLR
•HLA-G
decidualdendritic cells
•IL10
•IL4
•IL13
•TGF-beta
maternal blood vessel
glandular epithelial cells
•Glycodelin
•Galectin
uterine NK-cells
•VEGF
•IFN-gamma

Uterus ve dolaşımdaki NK hücreler

NK hücreler periferik lenfositlerin %5-10
uterus lenfositlerin % 70

-Yüzey spesifik markerları var(CD 56,19 vb)

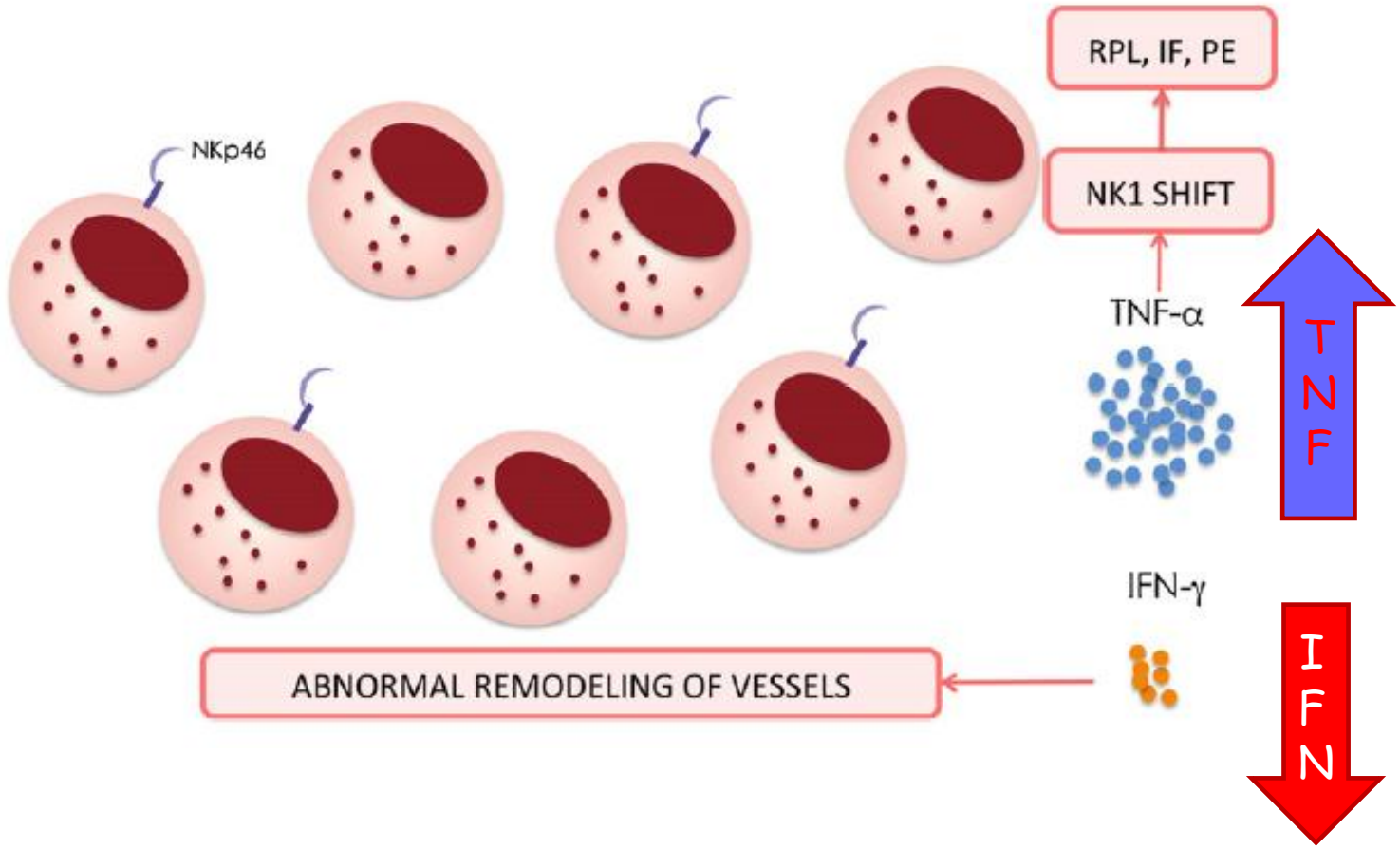
-Alt grupları $CD56^{bright}$ or $CD56^{dim}$ NK

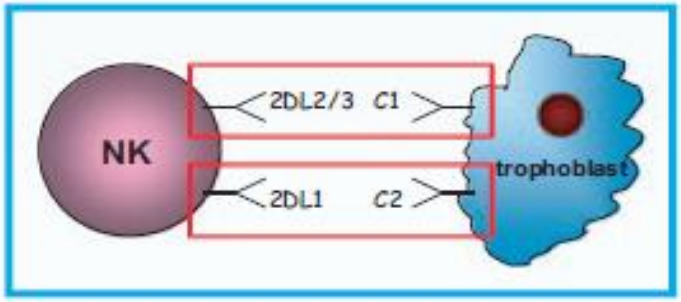
-Uterus NK hücreler $CD16^{-}/CD56^{bright}$

-Periferik NK hücreler $CD16+/CD56^{dim}$

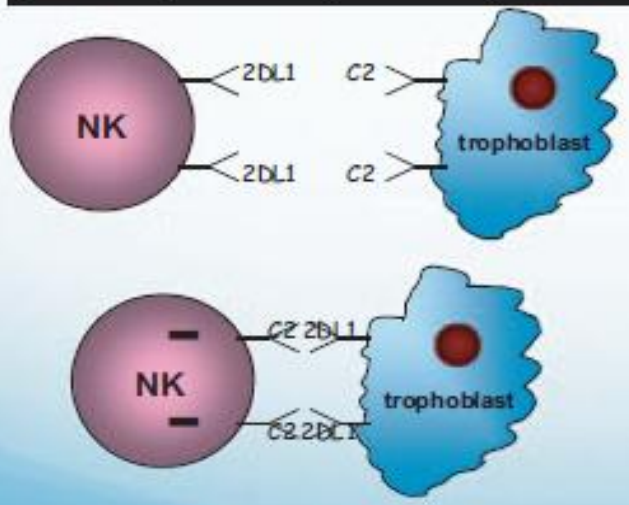
Periferik NK hücre ölçümü uterus NK larını yansıtır mı???

Natural cytotoxicity receptors and NK cell-producing cytokines in reproductive failure.



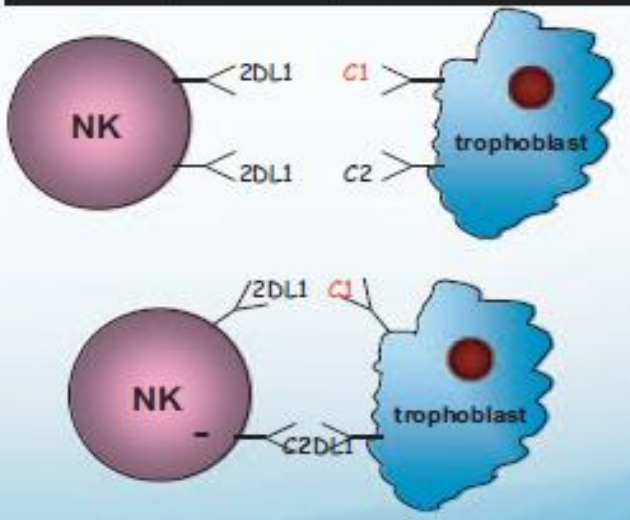


	Mother	Father	Fetus
HLA-C	HLA-C2 HLA-C2	HLA-C2 HLA-C2	C2/C2
KIR	KIR2DL1		



No killing

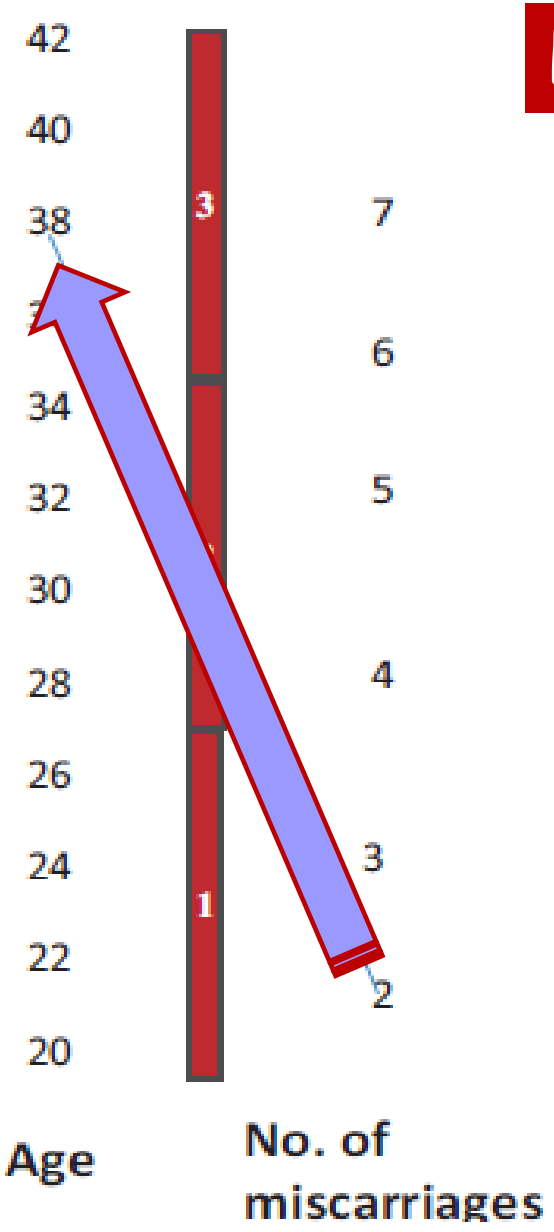
	Mother	Father	Fetus
HLA-C	HLA-C2 HLA-C2	HLA-C1 HLA-C2	C1/C2 C2/C2
KIR	KIR2DL1		



Potential killing

Killer cell immunoglobulin-like receptors (KIRs)

Basitten karmaşığa doğru testler



Assay Tests 1	Assay Tests 2	Assay Tests 3
Auto-antibody testing	NK Assays	HLA-c measurements
Anti-phospholipid Antibody testing	Cytokine Assays	KIR/KAR,

Recurrent Miscarriage and Cervical Human Papillomavirus Infection

Carl
Emi
[1]Aca
[2]Dep

Table I Prevalence of HPV DNA in Study Women

	Group 1 (RM)	Group 2 (Controls)
Women	*n* = 49 (%)	*n* = 475 (%)
HPV DNA Test +	13 (26.53)	294 (61.89)
HPV DNA Test −	36 (73.47)	181 (38.11)

$\chi^2 = 22.895$; $P < 0.001$.

Women with RM have a lower prevalence of HPV+DNA tests than controls. This suggests that immune reactivity potentially leading to RM could be in some way protective against genital HPV infection.

İmmunomodulatör tedaviler

1. Glikokortikoid
2. IVIG
3. İntralipid
4. Anti-TNF

Gkikokortikoidler

- Proinflamatuar sitokinleri inhibisyonu veT hücre ve NK supresyonu
- APAS de heparin ve aspirin ile kombinasyonu heparin ve aspirin ile aynı, ancak prematurite ve gestayonel diabet fazla çıkmış. Empson et al. (2005)
- 20 mg prednisolon+ 20mg Progesteron + aspirin + folik asit faydalı bulunmuş Tempfer et al. (2006)

A systematic review of intravenous immunoglobulin for treatment of unexplained recurrent miscarriage

Baris Ata, M.D., M.Sc., Seang Lin Tan, M.D., M.B.A., Fady Shehata, M.B., B.Ch., M.Sc., Hananel Holzer, M.D., and William Buckett, M.D.

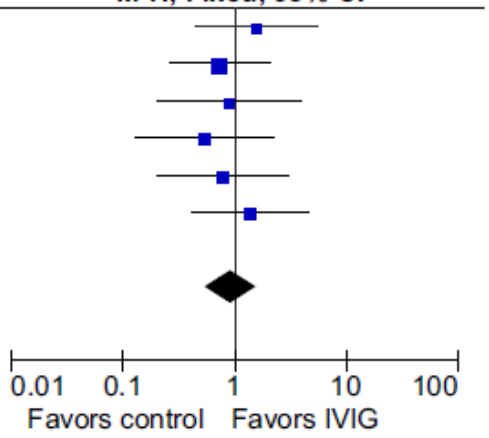
FIGURE 1

Live birth rate with IVIG in women with recurrent miscarriage.

Study or Subgroup	IVIG Events	IVIG Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Coulam 1995	10	21	7	19	12.6%	1.56 [0.44, 5.53]
German RSA/IVIG 1994	20	33	21	31	28.0%	0.73 [0.26, 2.05]
Jablonowska 1999	17	22	15	19	12.0%	0.91 [0.20, 4.01]
Perino 1997	16	22	20	24	17.1%	0.53 [0.13, 2.22]
Stephenson 1998	9	18	9	16	15.6%	0.78 [0.20, 3.01]
Stephenson 2010	16	23	15	24	14.7%	1.37 [0.41, 4.61]
Total (95% CI)		**139**		**133**	**100.0%**	**0.92 [0.55, 1.54]**
Total events	88		87			

Heterogeneity: Chi² = 1.89, df = 5; I² = 0%

Test for overall effect: Z = 0.30

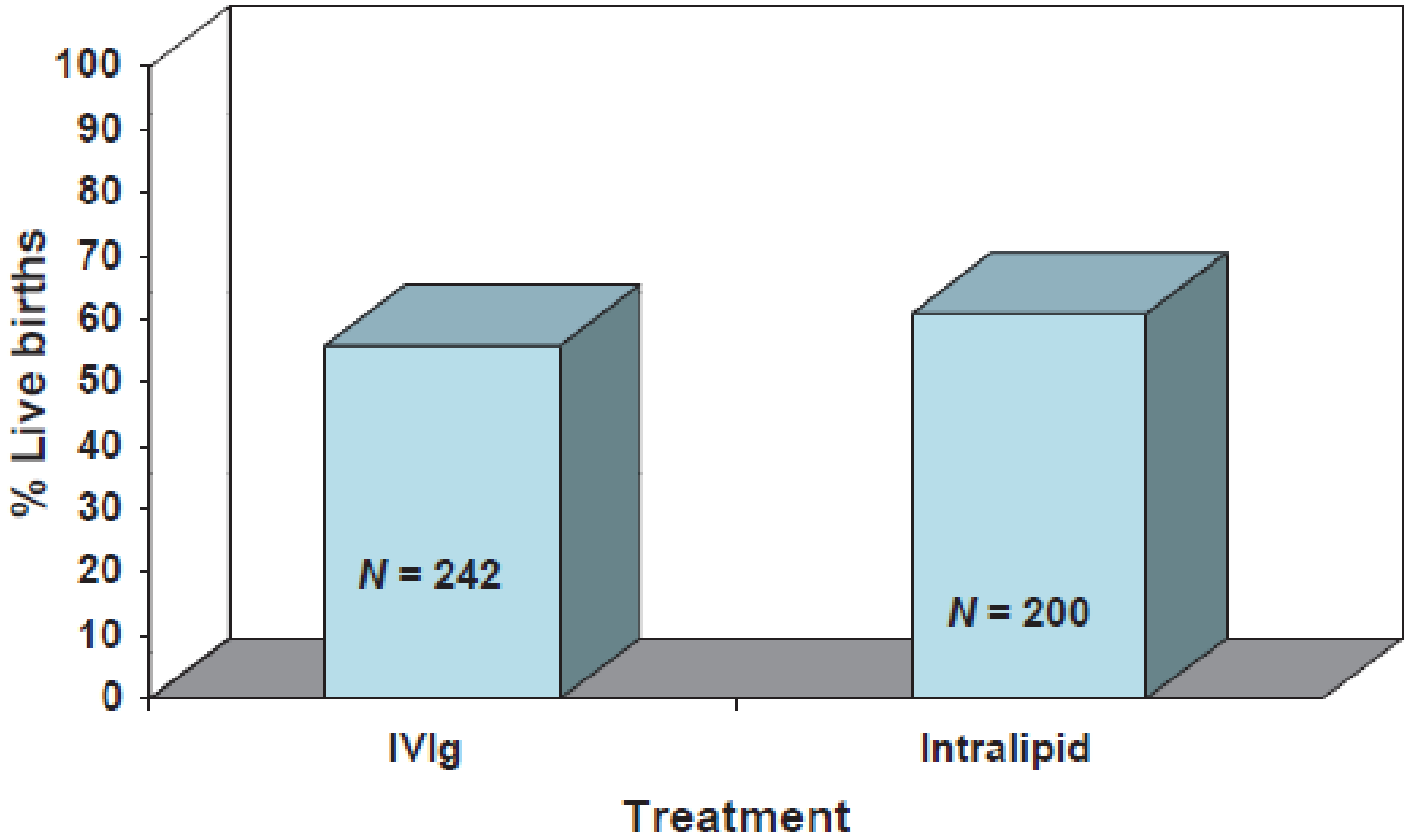


Ata. IVIG for recurrent miscarriage. Fertil Steril 2011.

Does Immunotherapy for Treatment of Reproductive Failure Enhance Live Births?

Carolyn B. Coulam[1], Brian Acacio[2]

[1]Reproductive Medicine Institute, Evanston, IL, USA;
[2]Acacio Fertility Center, Laguna Niguel, CA, USA



Human Reproduction, Vol.24, No.11 pp. 2703–2708, 2009
Advanced Access publication on July 17, 2009 doi:10.1093/humrep/dep240

human reproduction

ORIGINAL ARTICLE *Early pregnancy*

imulating

Results: In the group treated with G-CSF, 29 out of 35 (82.8%) women delivered a healthy baby, whereas in the placebo group, this figure was only 16 out of 33 (48.5%)

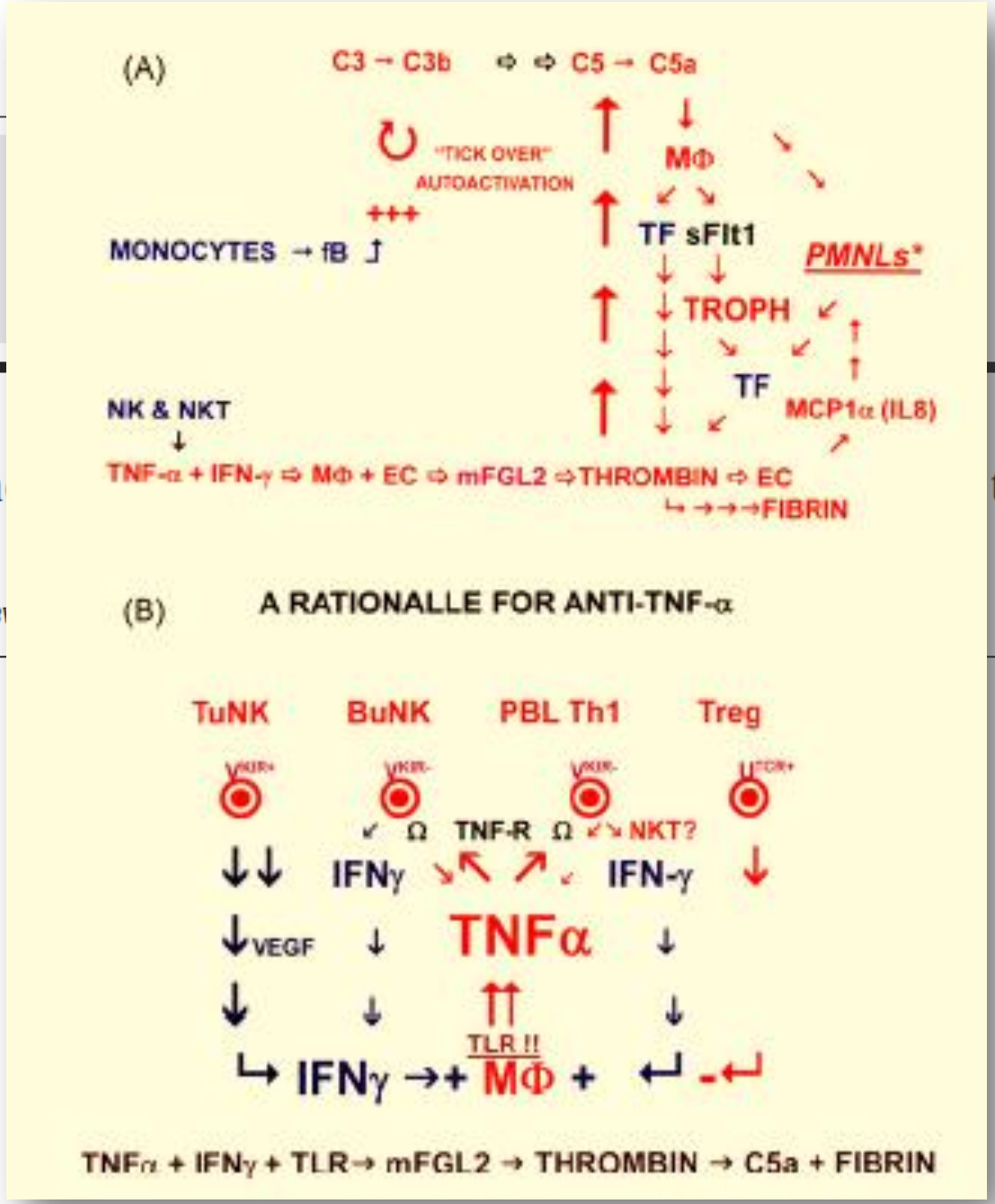
women with recurrent miscarriage (RM) treated with granulocyte colony-stimulating factor (G-CSF) ($n = 29$), women with RM treated with a placebo ($n = 16$) and normal pregnant women ($n = 15$). A statistical significant difference was observed ($P < 0.001$) in all weeks between the experimental group versus the placebo and normal pregnant women.

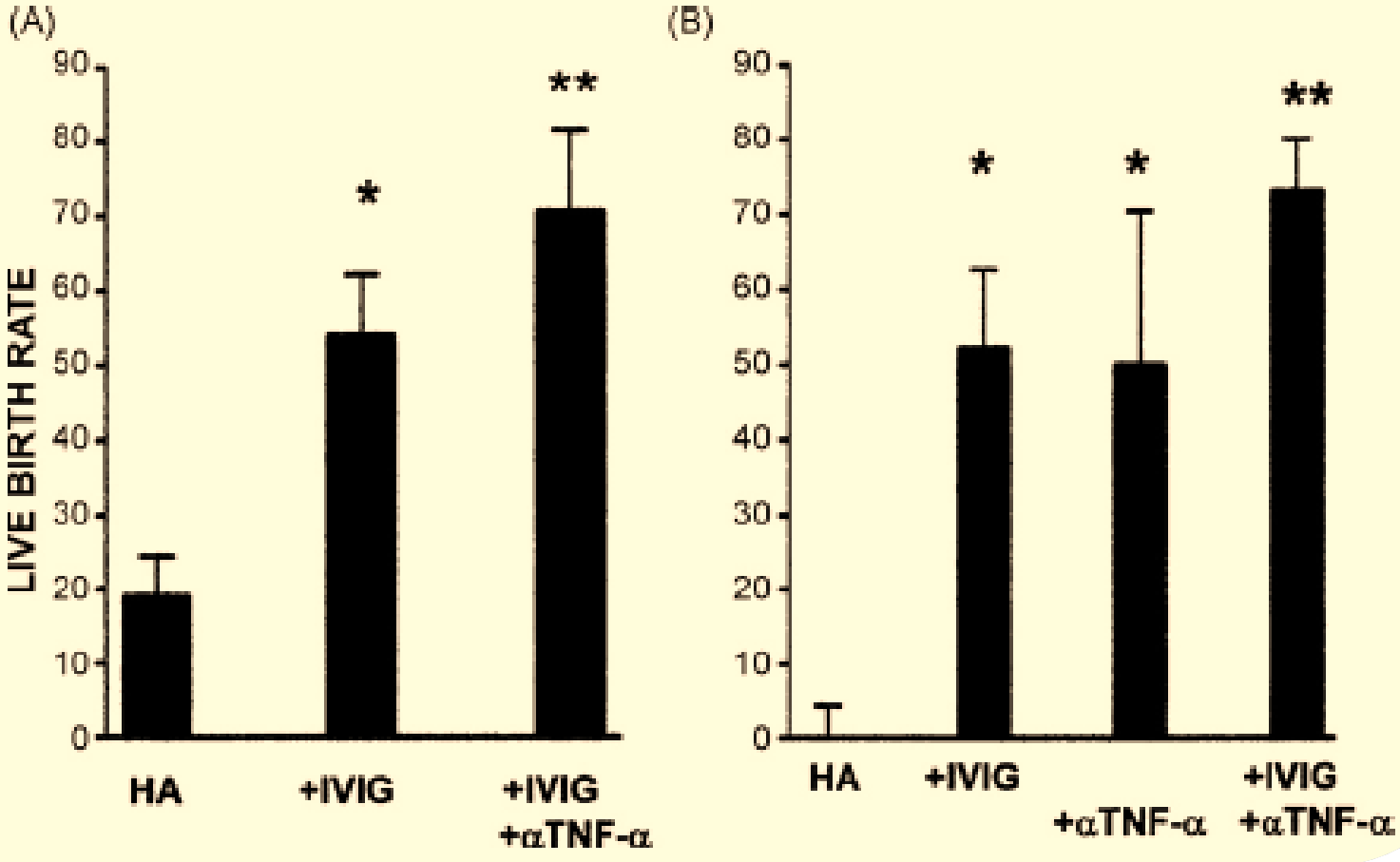
ELSEVIER

Anti-TNFα th… the art☆

David A. Clark*

McMaster University Room 3…





Summary results from clinical trials of
heparin + aspirin (HA) alone or
in combination with IVIG and/or anti-TNF drugs
(A) Recurrent spontaneous abortion results (Winger and Reed, 2008).
(B) Infertile IVF failure patients (Winger et al., 2009a).

Tümor nekrozis faktör alfa (TNF-a) inhibitörleri

Fiyatı : 2.263,16 TL

etanercept

Fiyatı : 1.001,63 TL.

infliksimab

Fiyatı : 1.033,38 TL

golimumab

Fiyatı : 2.030,57 TL

ELSEVIER

AUTOIMMUNITY REVIEWS

Review

Progester

Grant C. Hu

University of Washi

Cell Type		Reported effects	iPRs	mPRs
Granulocytes	Neutrophils	⬇ superoxide release ⬇ apoptosis ⬇ chemotaxis		
	Eosinophils	⇧ degranulation;		
	Mast cells	⇧ uterine infiltration (? direct)	H	
NK Cells		⇧ apoptosis (iPRs) ⬇ IFN-γ (iPRs) ⬇ cytotoxicity (indirect: via HLA-G, PIBF)	H	
Macrophages		⬇ nitric oxide ⬇ TNF-α ⬇ FcγR expression (MPA) ⬇ microparticle release	H	
	Myeloid DCs	⇧ ⬇ IL-10 ⬇ TNF-α, IL-6	r	
B cells		⬇ class switch recombination (iPRs) ⬇ T-dependent Ab responses (iPRs, ? direct) ⇔ altered Ig glycosylation	m	

PROGESTERONE ÖNEMLİ BİR IMMUN MODULATÖRDÜR

NELER DENENEBİLİR ?

İmmunomodulasyona yardımcı tedaviler

- Antibiyotik(makrolid)
- salbutamol, salmeterol and formoterol, (Th1 aktivitesi azaltıcı and Th2 artırıcı)
- D vitamini (immün regülatör)
- Tiroksin (eutroid, troit otoimmünitesi)
- Glikokortikoid ??? Aspirin + Folik asit+ didrogesteron

human reproduction ORIGINAL ARTICLE *Psychology and counselling*

Supportive care for women with unexplained recurrent miscarriage: patients' perspectives

Table I Preferred supportive care options for women with unexplained RM during next pregnancy (n = 15).

Domain 1: Medical supportive care	Domain 2: Non-medical supportive care	Domain 3: Other types of supportive care
Make a plan for the first 12 weeks with their gynaecologist	From gynaecologist	Women prefer an increase in partner involvement
Receive advice from their gynaecologist concerning life style, diet and internet sites	Enquire how the patient is doing and what her emotional needs are	The need for supportive care directly after a miscarriage
Preference of one or max two well informed gynaecologists	Take the women seriously	Feel unhappy in the waiting room with visibly pregnant women
	Give the women the feeling they are listened to and understood	
Receive frequent ultrasounds in early pregnancy and during symptoms	Counselling from social worker	
ßHCG blood monitoring before first ultrasound	Experiencing supportive care from family, friends and peer groups	
Receive medication only if it is safe for the child	Relaxation tools to unwind	
	Bereavement therapy for patients and explanation of bereavement levels for gynaecologists	

Table II **Miscarriage rates in women with untreated, unexplained RM (receiving supportive care alone) versus women in the general population.**

Study	Cases	Miscarriage rate (%)
Unexplained RM population[a]		
Stray-Pedersen and Stray-Pedersen (1984)	37	14
Liddell *et al.* (1991)	44	14
Vlaanderen and Treffers (1987)	20	20
Sheffield data (2011)	361	25
Brigham *et al.* (1999)	222	25
Clifford *et al.* (1997)	160	26
Total	844	14–26
General population		
Nybo Andersen *et al.* (2000)	513 832	12–25[b]

RM, recurrent miscarriage.

[a]Data from cohort studies where no treatment was given.

[b]Sporadic miscarriage rate for women aged 25–39 years.

İNCELEME	RCOG PROTOKOL	ACOG PROTOKOL	ESHRE PROTOKOL	ASRM PROTOKOL	HOLLAND PROTOKOL
PARENTAL KARYOTİP	**ÖNERİLİR**	**ÖNERİLİR**	**ÖNERİLİR**	**ÖNERİLİR**	**ÖNERİLİR**
FETAL KARYOTİP	**ÖNERİLİR**	YETERSİZ VERİ	YETERSİZ VERİ	YETERSİZ VERİ	**ÖNERİLİR**
APS ANTİKOR	**ÖNERİLİR**	**ÖNERİLİR**	**ÖNERİLİR**	**ÖNERİLİR**	**ÖNERİLİR**
UTERUS KAVİTESİ İNCELEME	**ÖNERİLİR**	**ÖNERİLİR**	**ÖNERİLİR**	**ÖNERİLİR**	**ÖNERİLİR**
TROİT ANTİKOR	ÖNERİLMEZ	ÖNERİLMEZ	**ÖNERİLİR**	ÖNERİLMEZ	
NK, HLA, CD56, T-HÜCRE	ÖNERİLMEZ	ÖNERİLMEZ	ÖNERİLMEZ	ÖNERİLMEZ	ÖNERİLMEZ

ÖZET

EŞLERİN KARYOTİPİ
HSG, SONO-HSG
APS ANTİKORLARI
TSH, HBA1c

TROMBOFİLİ TESTLERİ,
ANA, ANTİ-TG, NK, CD-16, HOMOSİSTEİN,
FETAL KARYOTİP İLE

KAFANI KARIŞTIRMA

GEBELİK ŞANSLARI OLDUĞU VE GEBELİĞİ DENEMELERİ ÖNERİLİR

DESTEK TEDAVİSİ(TLC) ÖNERİLİR

BEKLEYEMEYECEK VE PARASI OLANLARA İMMUNOMODULATUAR TEDAVİLER DENENEBİLİR.

Practice Committee. Recurrent pregnancy loss. Fertil Steril 2012.


TEKRARLAYAN
GEBELİK
KAYIPLARI
Prof. Dr. Sedat Kadanalı
nobel


Teşekkürler