

Confirmation Form Tanımlama Eşeli

Bölüm

4

An inflammation form SMILEYS, for clinical use, grounded on Claus Steuernagel concept*

Claus Steuernagel tablosu temelinde oluşturulan bir inflamasyon çizelgesi, SMILEYS*

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**This form is established for PPRM infants, and Presented at Prague, 2006, Perinatology Congress, as: Short and Long-Term Outcome of Premature Rupture of Membrane (PRM) Infants*

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This form is gathered parameters on inflammation reactions, thus, taken from the Claus Steuernagel concepts taken from Web. From the classical notifications; RUBOR: redness, CALOR: heat, TUMOR: swelling, DOLOR: pain and Dysfunction, mal function, and Type I, II, III and IV systems to inflammation mechanisms established perceptions.

Bu oluşturulan form, inflamasyon reaksiyonlarını bir araya parametreleri toplamak amacını gütmektedir. Claus Steuernagel Formu kullanılarak, eklemeler ile oluşturulmuştur. Klasik inflamasyon parametrelerini; kızarıklık, ısı, şişlik, ağrı ile işlev bozukluklarından, 4 tipin de form üzerinde belirtilmeye çalışılmıştır.

Systemic consideration is established, the parameters be in a single form, collected and get together for easy establishing these findings and give some clue on what will be required for laboratory examination and leading the clinical outcome, for treatment and also for taken care, and future perspectives.

This SMILEYS Form is used retrospective chart evaluation of PPRM cases, thus

the efficiency and the assisting the physician. Prospective meaning is not exactly indicate the efficiency and effectiveness, thus, retrospective demonstrates this aspect. Eligibility is noticed by the filling of the form one, thus, indicates, the Form is some educational considerations for the physician. Required some study indicated at the Form, whether these aspects are being at the patient or not.

Outline

An inflammation form for clinical use, grounded on Claus Steuernagel concept

AIM: Inflammation mechanisms are a multiple system considering concept, they were clustering effect mediated by; cytokines, enzymes, monoamine molecules, chemokines, eicosanoids, prostacyclin's, and several tissue parameters effect themselves.

Grounding Aspects: Claus Steuernagel (Web: 2001 Claus Steuernagel MD ©) indications and this first Unit "Infection-inflammation mechanisms/ *İnfeksiyon-inflamasyon mekanizmaları*" is the main grounding knowledge for establishing the SMILEYS Form.

Introduction: The reasoning to establish a form are; diagnostic scoring, knowledge based tables, grouping the evidences for clinical evaluation. The SMILEYS form includes all the all of them. This is not a simple yes or no, or scoring one, evaluation is required.

Notions: There are six parameters; 1) the severity of the inflammation, 2) principles of inflammation mechanisms, 3) clinical findings, 4) laboratory results, 5) predicts on inflammation, 6) evaluation due to the scoring.

Conclusion: PPRM cases, 100 cases at the gestation and 100 newborn infants, for control cases, are scored by this SMILEYS Form, considering the benefit of this Form. This Form is required special Proficiency for true evaluation of this problem, PPRM.

Key Words: Inflammation Form, Claus Steuernagel predict

Özet

Claus Steuernagel tablosu temelinde oluşturulan bir inflamasyon çizelgesi

Amaç: İnflamasyon mekanizmaları çeşitli sistemlerin birbirleri ile bağlantılı ve etkileşim içinde olduğu bir oluşumdur. Sitokinler, enzimler, mono-amin moleküller, kemokinler, eikosanoidler prostasiklin ve ayrıca doku reaksiyonları mekanizmaları başlatabilmektedir. Bu açıdan tablo genel anlamda tümünden irdelenmelidir.

Dayanaklar/Kaynaklar: Claus Steuernagel tablosu temelinde (Web: 2001 Claus Steuernagel MD ©), Birinci Ünite de belirtilen "*İnfeksiyon-inflamasyon mekanizmaları*" çalışmasına dayanılarak, SMILEYS Formu hazırlanmıştır.

Genel Yaklaşım: Bir form oluşturma amacı, tanısal bir kottama, tanısal bilgi sorgulama ve gruplama amacını gütmektedir. SMILEYS Formu, tüm bu amaçlara hizmet etmektedir. Ancak, bilimsel uzmanlık olması ile doğrusal boyuta ulaşılabileceği de kabul edilmelidir. Basit olarak var ve yok ile puanlama şeklinde bir tanımlama yapısında değildir, yoruma dayalıdır.

Yaklaşım: Başlıca 6 gruptadır; 1) inflamasyonun şiddeti, 2) inflamasyon mekanizmaları, 3) klinik bulgular, 4) laboratuvar sonuçlar, 5) inflamasyon öngörülere, 6) formdan elde edilen puana göre yorumlama.

Sonuç: Gebelikte PEMR-Preterm Erken Membran Ruptürü (PPROM) olgularında sırasına göre, bu problemi olan ve olmayan şeklinde ayırarak, 100 EMR sorumlu ve 100 EMR sorunu olmayan gebelik ve bebek geriye dönük bakılarak, formun yararlılığına uygulama ile bakılmıştır.

Yorum: Form uzman düzeyinde ve yorumlanması beceri ve medikal bilgi gerektirdiği görülmüştür.

Anahtar Kelimeler: İnflamasyon Formu, Claus Steuernagel tanımlaması

Primer

For a direct target to exact hit, first you **must** consider from the birth view, even to evaluate from complete body. Physical examination, even a skin problem, physicians inspect all the body, and also taken medical history at detailed aspect.

By this approach, we are considering all the inflammation process, under mechanisms of the inflammation, in a form, for taken in notice.

The Inflammation Form

This Form is established under such headings:

- 1) S: Severity of the inflammation
- 2) M: Mechanisms of the inflammation
- 3) I: Inflammation outcome: clinical findings
- 4) L: Laboratory results
- 5) E: Estimation of the inflammation
- 6) S: Score, obtained, and evaluation

Evaluation Criteria's

- 1) Inflammation Mechanisms: IMBALANCE
 - a. I: Infection
 - b. M: Mediatör Release
 - c. B: Blood Coagulation
 - d. A: Apoptosis
 - e. L: Labile, super-antigen
 - f. A: Antigen Presentation
 - g. N: Neutrophil Activation
 - h. C: Complement System
 - i. E: Effect on Tissue
- 2) Severity of Clinical Findings: FUNCTIONAL
 - a. F: Functional Variation
 - b. U: Unacceptable Adaptation
 - c. N: Non-destructive disturbances
 - d. C: Compensation period
 - e. T: Tissue Reactions Started
 - f. I: Impairments Noticed
 - g. O: Oxidative Stress, degeneration
 - h. N: Noticeable Finding
 - i. A: Abnormal Tissue Reactions
 - j. L: Lysis, and cellular, tissue death
- 3) Severity of Laboratory Results: NOTABLE
 - a. N: Negative
 - b. O: O, zero level
 - c. T: Trigger level
 - d. A: Appearance of the disease
 - e. B: Brief evident
 - f. L: Label of disease, diagnostic
 - g. E: Excess result

Reasoning to use the Form: SMILEYS

Reasoning to use this Form SMILEYS are:

- 1) Concerns all the parameters, concerning infection, inflammation and allergic problems. Even if some is not confirmed at the form, can be adding, thus, for each mechanisms section there is a space as indicated as: ***Other Findings***.
- 2) The severity of the problems, conditions and laboratory results are not only divided as, negative, positive; minimal, moderate and severe. The differentiation of the evidences at clinical findings grounding as from; functional adaptation to lysis and death.
- 3) For laboratory results, the evaluation is even different group. From negative, not known, not discriminate to minimal to excessive.
- 4) Causes, tissue and organ findings can be noted; thus, the expected conditions/problems are also indicated at this form.

1. F: Functional variations
2. U: Unacceptable adaptation
3. N: Nondestructive disturbances
4. C: Compensation period
5. T: Tissue reactions started

6. I: Impairments noticed
7. O: Oxidative Stress and Degeneration
8. N: Noticeable findings
9. A: Abnormal tissue reactions
10. L: Lysis, Cell and/or tissue death

CHART 1/A: Evaluation of the inflammation by immunologic mechanisms: SMILEYS

I M B A L A N C E	Inflammation I: Infection M: Mediator Release B: Blood; coagulation A: Apoptosis L: Labile: Super antigen A: Antigen presentation N: Neutrophil activation C: Complement system E: Effects on Tissues	Cause	Findings	Tissue /organ	Severe	Finding	TOTAL SCORE
					F U N C T I O N A L	N O T A B L E	S C O R E

I	Infection	Ischemia/hypoxia	<ul style="list-style-type: none"> Blood gases: pH, pCO₂ Oxygenation: SAT, pO₂ Electrolytes: osmolality O₂ content, p50 Metabolic values: LA, PA Acid-base status, BE 				
			BP, Pulse, CVP, capillary refilling				
			Hypoxanthine, hyper-uricemia				
		Mucosal Damage	Edema				
			Spasm/vasoconstriction &/or vasodilatation				
			Laceration, early ulcer				
			Secretion, exfoliation				
			Hypotonic or irritable				
			Dysfunction: <ul style="list-style-type: none"> Distension, diarrhea, Hepatic dysfunctions Renal ischemia Cardiac ischemia Ischemic tissues 				
		Translocation of bacteria &/or toxins	Positive culture Positive smear Contamination Trans vaginal Cytology Pathological findings Others	Oral and throat Rectal/stool Skin/umbilical Ear Blood, CNS, Amniotic Fluid Others			
		Reperfusion	Pooling, Vasodilatation				
			Pallor, vasoconstriction				
		Oxidative Stress					
		Immunologic Evaluation (Basal Values)	Neutralizing Immunoglobulin's <ul style="list-style-type: none"> Endotoxin; Lipopolysaccharide =LPS, Teichoic acid =LTA IL-1, TNF 				
			Previous immunologic deficiencies				
			Clinical Handicaps: Preterm infant Malnutrition, IUGR Anemia				
		OTHER FINDINGS					

M	Mediator Release	cAMP effects	<ul style="list-style-type: none"> Beta (2) adrenergic agonists () <ul style="list-style-type: none"> Ibuprofen &/or Vit C response Beta (2) catecholamine effects Acet salicylic acid effects (kinase) 				
		Immunologic Evaluation	<ul style="list-style-type: none"> IL-6, IL-8, IL-1B, TNF alpha IL-10 Toll Like Receptors (TLR) CD 14 LBP, etc <ul style="list-style-type: none"> Lipopolysaccharide Binding Protein (LBP) 				
		Mediator Effects	<ul style="list-style-type: none"> Edema, urticaria, toxic neonatal eruptions Vasodilatation, flushing Itching Irritability, diarrhea, 				
			Dysfunction: <ul style="list-style-type: none"> Abdominal compartment syndrome Hepatic functions 	.			
		OTHER FINDINGS					

“0”: None/negative

“?” = N/a

“+” = Suspicious

“++” = Slight

“+++” = Obvious

“++++” = Severe, “+++++” = Excess

1. F: Functional variations
 2. U: Unacceptable adaptation
 3. N: Nondestructive disturbances
 4. C: Compensation period
 5. T: Tissue reactions started

6. I: Impairments noticed
 7. O: Oxidative Stress and Degeneration
 8. N: Noticeable findings
 9. A: Abnormal tissue reactions
 10. L: Lysis, Cell and/or tissue death

CHART 1/B: Evaluation of the inflammation by immunologic mechanisms, SMILEYS

B	Blood; coagulation	<ul style="list-style-type: none"> DIC Fibrinolytic conditions: Factor II a, X a, IXa, VII Tissue Factors Thrombocytopenia HELP Syndrome 	petechia, ecchymosis, hemorrhage, bleeding	Plasma cascade --Complement --Kinin system --Fibrinolytic system --Coagulation cascade --Membrane attack Complex						
		OTHER FINDINGS								
A	Apoptosis	<ul style="list-style-type: none"> Cell death (Thrombocytopenia) Immunologic Evaluation 								
		OTHER FINDINGS								
L	Labile: Due to super antigen	<ul style="list-style-type: none"> Anaphylaxis Sudden alpha & beta receptor collapse Not primary response; MHC-II, T cells Fas ligand-perforin Immunologic Evaluation 								
		OTHER FINDINGS								
A	Antigen presentation	<ul style="list-style-type: none"> Th cells B cells and plasma, macrophages 	(Antigen Presenting Cells = APC)							
		Immunologic Evaluation	Specific increase; IgM, IgG							
		OTHER FINDINGS								
N	Neutrophil activation	<ul style="list-style-type: none"> Adhesion: accumulation of PMN Adhesion & phagocytes: MAS, LE cells Endothelial destruction; ulcers, exama Trans migration 		Cellular Reactions --Entothel adhesion --Transmigration --Chemotaxis						
		Organ Involvement	Skin problems, diaper dermatitis Hepatomegaly; Splenomegaly Omphalitis Diarrhea Conjunctivitis Others:							
		Immunologic Evaluation	TNF alpha, IL-1, C5a, C3a, Fas ligand, perforin							
		OTHER FINDINGS								
C	Complement system	<ul style="list-style-type: none"> Complement activation; C1, C3, C5 Acute Phase Reactors; CRP Membrane attack complex; Coombs positive 								
		OTHER FINDINGS								
E	Effects on Tissues	<ul style="list-style-type: none"> Ear, nose, throat Scalp, skin Eye Umbilical Pulmonary Abdomen Heart General Tissue Factors 	Rhinitis, URTI Dermatitis, diaper dermatitis Conjunctivitis Omphalitis Pneumonia Abdominal compartment synd. Myocardial Depression Factor Sepsis Syndrome	RUBOR: redness CALOR: heat TUMOR: swelling DOLOR: pain Dysfunction, mal function						
		OTHER FINDINGS								
9	TOTAL	per 9		per 9		per 9		_in9	_in9	+ /9

Sayfa. 171
 “0”: None/negative
 “?” = N/a
 “+” = Suspicious

“++” = Slight
 “+++” = Obvious
 “++++” = Severe, “+++++” = Excess

- 5) It is give a clue, what test and to which organ system must be evaluated. You can have focused the organ and the results for discussion of the people.
- 6) It makes you an argument, the findings that result of an inflammation mechanism. This means you must be considered the physio-pathological grounding of them. For further evaluation and outcome, the survey or the expectation of the disease.
- 7) The pointing has to be balanced. If considered under the evaluation. This from 10 points at FUNCTIONAL; 1-4 compensation status, 5-7 obviously have problem, must be solved, 8-10 treatment means a lifesaving, emergency aspects.
- 8) Laboratory results evaluation are; 1-2 negative, 3-4 slight, starting the reactions, 5-6 obvious, thus, 7 is excessive, be in danger.
- 9) Total Score evaluation; If the score, even for one mechanism is over 5 or 6 at 10, 4 at 7, the confirmation is YES, if less than these parameters, be aware and consider the classical aspects as; redness, pain, heat, swelling, disturbing the function. If there is some suspicious state, be follow the mechanism, whether to be in some way demonstrate a problem or disturbed function.
- 10) The Form is also an educational perspective for the physician, when try to filling, questioning for yes or no, requires searching.

Some Slides concerning SMILEYS

First the functional stages of the tissue/cellular problems.

Physio-pathological stages, from biological variation to death

Clinical Findings according to Severity		
1. F	Functional variations	Biological variation: Variations between the gestational ages and infants.
2. U	Unacceptable adaptation	Physiological adaptations try to control: Adaptation mechanisms, stimulus and feedback forced to control the body.
3. N	Non destructive disturbances	Functional disturbance: Increase in respiration, deep breathing, heart rate etc. No any injury. Metabolic activity increases.
4. C	Compensation period	Compensation: Compensatory phase of acidosis and alkalosis. Metabolic problems.
5. T	Tissue reactions started	Reaction of tissues started: Vasoconstriction, pooling, interstitial edema, central flowing of blood and systemic inflammatory reactions started.
6. I	Impairments noticed	Disturbances begin Cellular functions will be delayed, halted, ineffective and reactive states (e.g. Hypoxic Ischemic Encephalopathy (HIE) begin.
7. O	Oxidative Stress and Degeneration	Degeneration Vacuolar, hydropic cells and vasogenic edema develops. Histo-pathological findings are noticed. Changes in mitochondria
8. N	Noticeable findings	Clinical inflammation reactions are noticed: Fever, swelling, pain, etc are encountered.
9. A	Abnormal tissue reactions	Tissue reactions Tissue reactions, degenerations, hemorrhages, scleredema, cytostatic edema, Graft Versus Host, fibrosis.
10. L	Lysis Cell and/or tissue death	Cell and/or tissue death Lyses of erythrocytes, necrosis.

Figure 1: Stages of Clinical Findings and physio-pathological conditions

Figure one, is the reactional state of the diseases in general, form biological, individual variations, thus, each person, everyone has specific reactions. In here indicates ad gestational states, preterm, term and pot term and below 1000grams, 1500 gram, 2500 grams and

immaturity, Intrauterine Growth Retardation etc. Because it is first prepared for PPROM study.

The second step is to discriminate the evidences, from normal, slight to worse.

The biological discrimination of the results; negative to severe

Clinical Findings according to Severity			Causative Tissue Reactions/Cellular Response				
LEVEL	Positive	CLINICAL INDICATION					
N	- 0	Negative result	Slight	1	2	4	6
O	?	O level, not taken, not known the result					
T	+	Trigger level, Sub clinical, under required level	Moderate	3	4	6	8
A	++	Appearance of disease and/or laboratory results (Recorded level)					
B	+++	Brief evident, obvious level, diagnostic findings	Severe	4	7	9	10
L	++++	Label of disease, indicative, diagnostic clinical and/or laboratory finds					
E	+++++	Excess, overindulgence, mortal		Minimal	Recordable	Severe	Necrosis/shock

Figure 2: Evidence or Causative Factor and Tissue Response

I M B A L A N C E	Inflammation	F I N D I N G S	E V I D E N C E	OB/GYN & NEONATAL FINDINGS	F U N C T I O N A L	C O D E	R E S U L T S
	Infection						
	Mediator Release						
	Blood; coagulation						
	Appetite						
	Labile Type antigen						
	Antigen presentation						
Neurological activities							
Complement system							
Effects on Thymus							

I	Infection	Ischemia/hypoxia
		Mucosal Damage
		Translocation of bacteria &/or toxins
		Reperfusion
		Oxidative Stress
		Immunologic Evaluation (Basal Values)
		OTHER FINDINGS

M	Mediator Release	cAMP effects Tachycardia BP low or high
		Immunologic Evaluation
		Mediator Effects •Edema, urticaria, toxic neonatal eruptions •Vasodilatation, flushing •Itching •Irritability, diarrhea,
		Dysfunction: •Abdominal compartment syndrome Hepatic functions
		OTHER FINDINGS

B	Blood; coagulation	•DIC •Fibrinolytic conditions: •Factor II a, X a, IXa, VII •Tissue Factors •Thrombocytopenia •HELP Syndrome
		OTHER FINDINGS

Figure 3-a: The inflammation mechanisms; infection state, mediator release, blood and coagulation conditions.

A	Apoptosis	<ul style="list-style-type: none"> •Cell death (Thrombocytopenia) •Immunologic Evaluation 	A	Antigen presentation	<ul style="list-style-type: none"> •Th cells •B cells and plasma, macrophages
		OTHER FINDINGS			Immunologic Evaluation
					OTHER FINDINGS
L	Labile: Due to super antigen	<ul style="list-style-type: none"> •Anaphylaxis •Sudden alpha & beta receptor collapse •Not primary response; MHC-II, T cells •Fas ligand-perforin •Immunologic Evaluation 	C	Complement system	<ul style="list-style-type: none"> •Complement activation; C1, C3, C5 •Acute Phase Reactors; CRP •Membrane attack complex; Coombs positive
		OTHER FINDINGS			OTHER FINDINGS
N	Neutrophil activation	<ul style="list-style-type: none"> •Adhesion: accumulation of PMN •Adhesion & phagocytes: MAS, LE cells •Endothelial destruction; ulcers, exama •Trans migration 	E	Effects on Tissues	<ul style="list-style-type: none"> •Ear, nose, throat •Scalp, skin •Eye •Umbilical •Pulmonary •Abdomen •Heart •General •Tissue Factors
		Organ Involvement			OTHER FINDINGS
		Skin problems, diaper dermatitis			
		Hepamegaly;			
		Splenomegaly			
		Omphalitis			
		Diarrhea			
		Conjunctivitis			
		Others:			
		Immunologic Evaluation			
		OTHER FINDINGS			

Figure 3-b: The inflammation mechanisms; apoptosis, anaphylaxis, neutrophil activation, antigen-antibody formation, complement system, and tissue reactions.

For Evaluation and Discussion, from a research result on PPRM

Clinical Evidence FUNCTIONAL	PROM Negative n=56+6 t*=62							Total n	PROM Positive n=54+1 t*=45							Total n
	Inflammation reactions IMBALANCE								Inflammation reactions IMBALANCE							
	None n/a	1-4			5-9				None n/a	1-4			5-9			
		Severity			Severity					Severity			Severity			
		+	++	4+	+	++	4+			+	++	4+	+	++	4+	
None	10							10	8							8
1-5		3	2	2				7		1		1				2
6-10		1	4	5	1	7	27	55		4	2	1	11	17		35
TOTAL (n)	10	4	6	7	1	7	27	62	8	1	4	3	1	11	17	45
(%)	16.1	6.5	9.7	11.3	1.6	11.3	59.7	100	17.8	2.2	8.9	6.7	2.2	24.4	37.8	100

t* =sw n

✨ No findings in PROM + 17.8 to Negative 16.1%
 ✨ Minor complaints in PROM + 37.7 to Negative 29.1%
 ✨ Severe problems in PROM + 44.5 to Negative 71.0%

Figure 4: The PROM (Preterm Rupture of Membrane) positive and negative infants, and Maternal Inflammation evidences, and the clinical problems encountered as; minimal, moderate and obvious.

Yes, and yes indications mean 67,9% problem is confirmed, for early evaluation, before disease encountered, and meaning to be protect before severe and obvious and life-threatening stage.

Early estimation the inflammation and the severity before it is going worse

MOTHERS (n-%) PROM		INFANTS (n-%) Inflammation reactions IMBALANCE		
		YES	NO	TOTAL
Positive		36 – (81.8%)	8 – (18.2%)	44 – (100%)
Negative		46 – (82.1%)	10 – (17.9%)	56 – (100%)
	Other Inflammation YES	36 – (94.7%) [78.3%]	2 – (5.3%) [20%]	38 – (100%) [67.9%]
	Other Inflammation NO	10 – (66.7) [21.7%]	8 – (33.3) [80%]	18 – (100%) [32.1%]
Total (n-%)		46 – (82.1%) [100%]	10 – (17.9) [100%]	56 – (100%) [100%]

Figure 5: Mother and infant, thus, imbalance ratio as yes or no, even for other perinatal conditions, problems, diseases.

Conclusion

From the physician perspective, the evaluation and consideration, in order the finding and the laboratory evidence obtained from the patient. Then making a searching on them.

This SMILEYS Form, at inflammation, the other parameters, and the problem is connection with other evidences, thus some reactions in counter and similar effects, triggered a cluster of the reactions. Antigen presentation, later antibody formations, thus, needs a duration to be established, first IgM, so follow up IgG etc.

The balancing the degree and the severity, confirms the clinical status and the treatment stages, from protection to wide multi system treatment.

The PPRM evaluation results are also added, thus, PPRM study is considered at the flowing research. This might be a 10 years old evaluation, thus, still an example for this Form.