Original Article

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Clinical Manifestation and Diagnostic Approach Towards 'TORCH Test': A Knowledge, Attitude and Practice Study

Microbiology Section

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ABSTRACT

Introduction: 'TORCH Test' (Toxoplasmosis, Rubella Cytomegalovirus, Herpes simplex) is usually requisitioned in females having 'Bad Obstetrics History (BOH)' or those who are suspicious of 'intrauterine infection' or for neonates having congenital malformation. However, the understanding of the test is lacking amongst the practitioners. Hence, this Knowledge Attitude and Practice (KAP) study was conducted to access the knowledge of resident doctors about the correct way of requesting TORCH test.

Aim: To assess the understanding, clinical manifestation and diagnostic approach towards TORCH test amongst the Resident Doctors.

Materials and Methods: Four groups of questions were put to Resident Doctors from Obstetrics and Gynecology (ObG), Paediatrics (Paeds) and Microbiology Department to assess their understanding of TORCH test. The questionnaire having 30 questions was divided in four groups A, B, C and D. Group A (Q. 1-4) about the fundamental of TORCH infection; Group B (Q. 5-8) brief clinical manifestation; Group C (Q. 9-12) indication of TORCH test i.e., when torch test should be requested and Group D (Q. 13-30) result interpretation of TORCH profile.

Results: Questions as to the full form of TORCH test were correctly answered by almost all participants. As far as questions as to Clinical Manifestation, residents of ObG (72.3%) were more accurate in predicting than that of Paeds residents (48%). Amongst Microbiology residents only 5.2% of them were able to gave correct answers. When questions as to when the TORCH test is to be recommended were asked, only 30.7% residents of Paeds, 59% of ObG and 10.5% of Microbiology were aware about it. Interpretation of the test results amongst the participants was also not that up to the mark as only 36.1% in Paeds, 67.6% in ObG and 29.8% in Microbiology residents were correctly able to predict. To sum up, understanding, clinical manifestation and diagnostic approach towards TORCH test is better amongst the ObG residents (67.7%) as compared to that of the Microbiology Residents (26.7%) and Paeds Residents (42%).

Conclusion: It can be understood that since the clinical branch residents of ObG and Paeds are not that thoroughly acquainted with the TORCH test understanding and complete clinical information is necessary. Therefore, it is apparent that the same is being not requisitioned in cases where pregnant women or infants have non-descript illnesses where testing is not necessary at all. It is, therefore, highly recommended that regular seminars and teaching activities are conducted by the concerned respective departments in order to impart TORCH test understanding and complete clinical information regarding it.

Keywords: Antibodies, Bad obstetrics history, Resident doctors

INTRODUCTION

The TORCH test belongs to a category of blood tests about the infectious-disease antibody titer found in blood or serum that determines their level of concentration. The acronym TORCH is obtained from initial letters of the five chronic infections: Toxoplasmosis, Rubella, Cytomegalovirus (CMV), and Herpes Simplex Virus (HSV) [1]. Since then the acronym has been expanded, with the addition of syphilis (TORCHS), and Parvovirus B19, Enterovirus, Coxsackie virus, Epstein-Barr virus (mononucleosis), Hepatitis B and HIV as 'others' (CHEAP TORCHS) [2].

Together TORCH infections can cause a cluster of symptomatic birth defects known as TORCH Syndrome [3]. TORCH test is generally advised in the newborns with congenital malformation and in the females having 'BOH'. However, majorly the understanding of the test is lacking amongst the practitioners and therefore it is quite prevalent that the tests are being requisitioned indiscriminately causing thereby losses of resources. Due to the lack of understanding of the TORCH test, it usually happens that the practitioners from the ObG, Paeds usually advise the TORCH test when a newborn has congenital malformation or for females with BOH. It has become necessary to evaluate the utility of the TORCH test with the present understanding of TORCH agents and its clinical manifestations so as to ensure that the possibilities of confusions are eradicated and resources used up in the tests can be saved. This is the reason why TORCH test has become the most abused test [4]. It is well known that in clinical practices, the value of this testing has been questioned in numerous quarters [5-7]. According to Microbiologists, such requests are often inappropriate as the requests are not targeted appropriately [4].

The need for going ahead with this study arose from the fact that during working in Tertiary Care Centre, author experienced that a number of TORCH serology requests are received where it was found that request was not appropriate considering detailed history and clinical presentation of the patient. Hence, this KAP study was done to evaluate the knowledge of Residents working in Paeds, ObG and Microbiology Departments.

MATERIALS AND METHODS

This was a KAP type of study carried out in the month of March 2017 in which questionnaire was prepared and distributed to resident for study purpose and the assessment was done in April-May 2017 at Department of Microbiology, Dr SN. Medical College, Jodhpur, Rajasthan, India. The study did not involved any human procedures and therefore requirement of taking ethical clearance did not arise. However, consent from the participants, who were 73 Resident doctors, was duly taken.

Since the TORCH test is concerned majorly with the Department of ObG, Paeds and Microbiology therefore, 28 ObG residents,

26 Paeds residents and 19 Microbiology residents were included in the study and all others residents were excluded. Assessing the residents of the concerned departments would be the best way out to arrive at the conclusion of the study as the requisitions for the test is majorly received from them only.

Since it was a KAP study therefore, a questionnaire (which is '[Annexure 1]') consisting of 30 questions was designed by the author team taking into consideration all the aspects pertaining to TORCH test and TORCH infection which fulfills the aims and object of this study. This questionnaire was taken as an assessment tool for testing the understanding, clinical manifestation and diagnostic approach of resident doctors of the above referred departments about TORCH test. This questionnaire was reliable and valid as the questions were designed from standard books and published articals, keeping in mind, the objectives of study [4,8,9].

These questions were divided in four groups for conveniently understanding each aspect of the study namely, A, B, C and D. Group A ranging from (Q. No. 1 to 4) contained questions strictly concerning the fundamental understanding of the TORCH infection. Group B ranging from (Q. No. 5 to 8) contained questions strictly pertaining to clinical manifestation of the TORCH infection in pregnant women and neonates; Group C ranging from (Q. 9 to 12) contained questions strictly pertaining indications of TORCH test i.e. situations when this test is to be requested and Group D ranging from (Q. 13 to 30) contained questions pertaining to serological result interpretation of TORCH profile. Group A is knowledge based questions, Group B and C are attitude based questions and Group D is practice based questions.

This questionnaire was given to each Resident doctor as above and was collected after 30 minutes. Assessment on questions was done having criteria that whether the participant had knowledge of subject or not. Those answering the questions correctly were designated as 'K' and others (wrongly answered/incompletely answered/unanswered) with 'NK'.

STATISTICAL ANALYSIS

Descriptive analysis was done using MS Excel Statistical Package for the Social Sciences (SPSS) software version 22 and result were interpreted into percentage.

RESULTS

The study participants were 73 Resident doctors of age group 22-30 years which included 40 males and 33 females resident and all were 2nd and 3rd year Residents.

Group A Questions

This group of questions was focused only to determine the level of fundamental understanding of the TORCH test amongst the residents. Results show that the residents of the Paed and ObG Departments were quite aware about the basics of the TORCH test as almost 73% of residents of both these departments were able to correctly answer the questions. Only half of the residents of the microbiology department were clear on the fundamentals of the test which brought down the average of participants having knowledge of the test to as low as 66.8% [Table/Fig-1,2].

Question number	Paeds (26)		ObG (28)		Microbiology (19)		Total (73)	
	K	NK	K	NK	K	NK	K	NK
1	25	1	27	1	19	0	71	2
2	22	4	22	6	13	6	57	16
3	16	10	12	16	1	18	29	44
4	13	13	20	8	5	14	38	35
5	10	16	19	9	1	18	30	43
6	13	13	21	7	0	19	34	39
7	13	13	20	8	1	18	34	39
8	14	12	21	7	2	17	37	36
9	8	18	24	4	4	15	36	37
10	10	16	15	13	3	16	28	45
11	8	18	9	19	1	18	18	55
12	6	20	18	10	0	19	24	49
13	15	11	25	3	8	11	48	25
14	12	14	23	5	6	13	41	32
15	10	16	25	3	8	11	43	30
16	12	14	18	10	4	15	34	39
17	6	20	20	8	6	13	32	41
18	7	19	18	10	2	17	27	46
19	8	18	22	6	4	15	34	39
20	8	18	18	10	3	16	29	44
21	6	20	13	15	8	11	27	46
22	9	17	11	17	7	12	27	46
23	9	17	15	13	9	10	33	40
24	13	13	13	15	5	14	31	42
25	8	18	16	12	4	15	28	45
26	9	17	12	16	5	14	26	47
27	10	16	25	3	8	11	43	30
28	9	17	25	3	4	15	38	35
29	12	14	17	11	7	12	36	37
30	6	20	25	3	4	15	35	38
TOTAL	327	453	569	271	152	418	1048	1142

[Table/Fig-1]: Frequencies of Resident doctors who have knowledge/no knowledge about TORCH test questions.
K: Knowledge; NK: No knowledge

Group B Questions

From responses received to this group of questions it can be gathered that 48% and 72.3% of the residents from the Paed and ObG department respectively, were aware of the manifestations of the TORCH infection [Table/Fig-1,2]. Since, this group of questions were relating to clinical manifestation of the TORCH infection which is majorly a work profile of the residents of clinical branch, therefore apparently ObG and Paed residents being from clinical branch are much aware about manifestation of the infection. Still, it is noteworthy that residents of ObG department are much aware of it as compared to that of the Paed department residents. As far as the microbiology residents are concerned, only 5.2% of them were aware of such questions.

	Paediatrics residents (26)		Obstretic and Gyanae residents (28)		Microbiology residents (19)		Total	
	K	NK	K	NK	K	NK	K	NK
Group A Q. 1-4	76 (73%)	28 (27%)	81 (72.3%)	31 (27.7%)	38 (50%)	38 (50%)	195 (66.8%)	97 (33.2%)
Group B Q. 5-8	50 (48%)	54 (52%)	81 (72.3%)	31 (27.7%)	4 (5.2%)	72 (94.8%)	135 (46.2%)	157 (53.8%)
Group C Q. 9-12	32 (30.7%)	72 (69.3%)	66 (59%)	46 (41%)	8 (10.5%)	68 (89.5%)	106 (36.3%)	186 (63.7%)
Group D Q. 13-30	169 (36.1%)	299 (63.9%)	341 (67.6%)	163 (32.4%)	102 (29.8%)	240 (70.2%)	612 (46.6%)	702 (53.4%)
TOTAL	327 (42%)	453 (58%)	569 (67.7%)	271 (32.3%)	152 (26.7%)	418 (73.3%)	1048 (47.9%)	1142 (52.1%)

[Table/Fig-2]: Frequencies of Resident doctors who have knowledge about TORCH test according question group A, B, C, and D.
Group A (Q. 1-4) Question about the full form; Group B (Q. 5-8) brief clinical manifestation; Group C (Q. 9-12) Indication of TORCH test i.e. When torch test should be requested and Group D (Q. 13-30) result interpretation of following TORCH profile
K: Knowledge; NK: No knowledge

Group C Questions

This group of questions tests the participants on when they should prefer to conduct TORCH test. Majorly, this group of question is somewhat related to practical application of the knowledge of the manifestation of the disease during the test request. The need for this study has arisen majorly to evaluate the participants on this aspect because it is the step where test requests are made and here the alleged abuse of the tests can be avoided.

Performance of all the residents on this group of questions is not up to the mark as only 30.7% of Paed Residents, 59% of ObG and 10.5% of Microbiology residents were able to answer the questions correctly [Table/Fig-1,2].

Group D Questions

Once the tests requests are made, it becomes necessary that the results obtained from the procedure are interpreted correctly. Performance of the residents on this aspect is also not appreciable as only 36.1% from Paed and 29.8% of Microbiology were correctly able to interpret the results obtained from the procedure. However, 67.6% of the ObG residents were able to correctly interpret the results [Table/Fig-1,2].

To sum up, understanding, clinical manifestation and diagnostic approach towards TORCH test is better amongst the ObG residents (67.7%) as compared to that of the microbiology residents (26.7%) and Paeds residents (42%) [Table/Fig-1,2].

DISCUSSION

The aim of the study in specific terms was to bring down the rising number of TORCH test requests being received for pregnant woman with BOH and neonates having congenital malformation. This is majorly because of wrong indications and wrong interpretation of the test results due to inappropriate knowledge among Doctors. So before analysing the results obtained in this study, it is necessary to understand the clinical symptoms, serological diagnosis and result interpretation, limitation of serological testing and confirmatory/ more specific tests of each infections of the cluster.

Toxoplasma gondii

Clinical symptom-The symptoms of *Toxoplasma* e.g.. intracranial calcifications, skull and encephalic anomalies and eye anomalies are more commom than severe complications like thrombocytopenia, anemia, jaundice, hepatomegaly, Central Nervous System (CNS) sequelae [7,9].

Serological diagnosis and result interpretation-It is a established fact that when a woman is infected with a pathogen during pregnancy, the result is a normal immune response which results in the production of IgM (Immunoglobulin M) antibodies followed by IgG (Immunoglobulin G) antibodies. So formed, IgM, antibodies against TORCH organisms and they usually persist for about three months. But as far as the IgG antibodies are concerned they remain detectable for a complete lifetime, thereby providing immunity and consequently preventing or rather reducing the severity of chances of re-infection. Thus, it can be safely said that if IgM antibodies are found in a pregnant woman on a test made on her, it clearly establishes that a recent infection with the organism [10]. Also, negative to positive seroconversion of IgG antibody can indicate *Toxoplasma gondii* infection.

Limitation of toxoplasma testing-Limitation of this test lies in the fact that when *Toxoplasma* IgG is low in circulation in the body then there are chances that equivocal *Toxoplasma* IgG results may be obtained and there it becomes important that a second test is conducted. Single positive test for *Toxoplasma* IgG should not be used to diagnose recent infection.

A preterm baby may be infected with TORCH organism, yet may not demonstrate a IgM response. Even in a term baby with the congenital infection, IgM for TORCH infection in the cord blood could be negative in 19% with congenital toxoplasmosis despite definite intrauterine infection [11]. Confirmatory test is more specific test in case, when serial sampling is not possible/feasible, demonstration of IgG with low avidity index indicates a recent infection more specifically. Avidity is directly proportional to the time since the onset of infection so with passage of time, the avidity index increases. Presence of low avidity IgG is a strong predictor of foetal/neonatal infection. For toxoplasmosis an avidity index of <15% indicates a primary infection acquired within last three months; index between 15-29% is considered equivocal; while that above 30% is suggestive of the infection acquired more than six months back [12,13].

The causative organism can be isolated from placenta, serum, and cerebrospinal fluid [14]. If mother has evidence of acute infection, then diagnosis for the causative organism in the foetus can be performed more accurately within 18 weeks of gestation using Polymerase Chain Reaction (PCR) amplification of the B1 gene of *T. gondii* [15].

Rubella

Clinical symptom-During infection in pregnancy, mother can have symptoms such as fever, malaise, Upper Respiratory Tract Infection (URTI), conjunctivitis and lymphadenopathy. For chheimer's spots, Rubelliform rash (1-3 mm in diameter), encephalitis, arthralgia, thrombocytopenia, neuritis, orchitis etc. is looked for. Infant shows symptoms mainly microcephaly, micrognathy, cleft lip/palate, congenital heart defect (pulmonary artery stenosis, patent ductus arteriosus, ventricular septal defects, coarctation of the aorta) eye defects such asocular cataracts, microphthalmia, glaucoma, pigmentary retinopathy, microphthalmos, hearing defects, purpuric skin lesions (blueberry muffin skin) [8].

Serological diagnosis and result interpretation-Detection of IgG-class antibodies to rubella show prior exposure through infection or immunisation and it indicate that such women are immune. If result are equivocal than an additional specimen should be tested after two weeks to demonstrate IgG seroconversion if patient is recently vaccinated. If result are IgM positive, it shows acute infection and foetus at risk. Both IgG and IgM positive shows recent infection but the timing of infection should determined with avidity index.

Limitaion of Rubella testing-These results are not applicable for preterm baby and even in a term baby with the congenital infection as IgM in the cord blood, could be negative in 39% of term newborns with congenital rubella [16]. Specimens that are drawn early may indicate negative for IgG class antibodies during the acute phase of infection or shortly (1-2 weeks) following vaccination may be. Confirmatory test/ more specific test-The diagnosis of infection can be carried out using a virus, isolated from nasopharyngeal secretion. RNA probe and PCR are also used to detect the virus in amniotic fluid or chorionic villi [15].

Cytomegalovirus (CMV)

Clinical symptom-CMV infection is usually asymptomatic in 90% of cases in mother. Only mild symptoms like fever, fatigue, myalgia, hepatitis, lymphadenopathy can occur [9]. But as far as infants are concerned, they show various complications which may be optic atropy, microcephaly, hypotonia, intracranial calcifications, and decrease hearing, pneumopathy, thrombocytopenic purpura [9]. If the mother has a primary infection during pregnancy, foetal morbidity rate is high [15]. Patients with congenital CMV infection are more likely to experience post-natal seizures.

Serological diagnosis and result interpretation-If result are CMV IgM positive, it shows acute infection and foetus is at risk. Both IgG and IgM positive shows recent infection. In CMV virus, presence of IgG antibodies indicate past or recent exposure to infection. CMV transmit to susceptible persons through blood and tissue products. Presence of IgG in equivocal CMV may occur during acute infection or due to non-specific binding reactions. Additional specimen should be considered for testing if clinically

indicated. Negative CMV IgG results individuals are considered susceptible to primary infection.

Limitation of CMV testing-Early sera drawn from body during the acute stage of infection may not detect the level of CMV IgG. Even in a term baby with the congenital infection, 11% with congenital CMV fail to demonstrate an appreciable IgM response at birth, despite definite intrauterine infection [17]. In case of immunosuppressed or organ transplant recipients, results cannot be evaluated and have not been accepted for cord blood or for neonatal testing. False positive results produce because of non-specific binding of immune complexes or other immunoglobulin aggregates present in patient specimen. The cross-reactivity with human chorionic gonadotropin, HIV IgG, multiple myeloma IgG, rheumatoid factor IgM and *Toxoplasma gondii* IgG.

Confirmatory test/More specific test-For arriving at a perfect result, the tests of taking body fluids such as urine and pharyngeal secretions should be done within first three weeks after birth because thereafter it becomes quite difficult to decide whether the infection detected is congenital or post-natal infection [11]. PCR technique is very frequently used for detection of this virus [9].

Herpes Simplex Virus (HSV)

Clinical symptom-Infection can occur in neonates during birth through an infected vaginal canal and post-natal infection can be spread through infected persons by kissing or touching the infants. About half of the women having primary infection are asymptomatic. About 20% mothers show symptoms like vulvovaginitis and cervicitis and present with characteristic vesicular and ulcerated genital lesions. Infants show complications like: (a) Skin lesions: vesicles, vesiculobullous, ulcer, pustular, erythematous, and scarring; (b) CNS lesions: calcification, encephalomalacia, ventriculomegaly, microcephaly, haemorrhage, seizures, meningoencephalitis, and hypertonia/spasticity; (c) Eye lesions: keratoconjunctivitis, chorioretinitis, cataracts, retinal detachment [11].

Serological diagnosis and result interpretation-Presence of IgM antibody to HSV denotes a recent infection while presence of IgG antibodies indicates a past infection. Recent infection can be documented by demonstration of any of three: (i) organism specific IgM; (ii) four-fold rise in the organism specific IgG; or (iii) recent conversion from a seronegative to seropositive state [4].

Limitation of HSV testing-For HSV type 1 and 2, IgM/IgG is non-specific and has little clinical value as the presence of IgG-class antibodies to HSV indicates previous exposure so should not be used routinely as the primary means of diagnosing HSV infection.

Diagnosis-A clinical specimen such as oral, dermal, or genital lesion should be tested to detect HSV types 1 and 2 by rapid PCR and HSV culture in case of patients presented with presumed acute infection with HSV and the person considers to be infected, if the result of serum HSV IgM, HSV PCR of the CSF or HSV culture of lesions comes positive [18,19].

Apart from the above, recently, new diagnosis method Protein microarray has been introduced which is miniaturised, chip-based, microarray methods which permit measurement of many analysts from small quantity of samples and reagents which is more sensitive and rapid than conventional system. Microarray-based DNA analysis technologies are used to track the activity of thousands of genes at once [20].

TORCH infections in reality do not usually affect more than one pregnancy in the same mother. The chances of re-infection are almost none in rubella and extremely rare in toxoplasmosis but it does occur in CMV and herpes and in these infections the chance of a newborn carrying the infection from the mother ranges between 30-60%, and even lesser are the chances of the infected child being symptomatic [Table/Fig-3] [4]. There is a myth that TORCH should be investigated and diagnosed as an entity, but the truth is that pathogens are capable of congenital infection should be considered in view of clinical symptoms of the neonate, maternal vaccination status, standard early pregnancy screening and risk factors, such as travelling to endemic areas or sexual behaviour [21]. So, clinicians should be encouraged to send specimens for specific tests depending on the clinical features of individual cases not as a common investigative pathway (TORCH screening) and Investigations also need to be organism specific.

Infections	Infected foetus	Symptomatic infected mother
Toxoplasmosis	40%	20%
Cytomegalovirus	40%	15%
Rubella virus	60%	30%
Herpes simplex virus	30%	40%

[Table/Fig-3]: Risk of foetal infection and symptomatic neonatal infection in a mother infected with TORCH organisms.

Limitation(s)

As this study was performed with limited number of participants and single institute is involved so a larger involvements of doctors will be needed to conclusively link the serological diagnosis with maternal infections.

CONCLUSION(S)

As the cost of whole TORCH panel test is very high, it becomes impossible for general population of a developing country like India as they cannot comfortably afford this testing. It is irrational to order TORCH screening test as a blanket investigation and therefore clinicians should request these test depending on the clinical features of individual and pathogen and the results must be interpreted in conjunction with complete clinical information. TORCH testing should not be applied indiscriminately to pregnant women or infants. It not only decreases the cost to the patient but also decreases the effort and confusion. There should be regular teaching activities, seminar, lectures and group discussion on this topic to enhance and update the knowledge of residents, interns, medical students even the faculties of medical profession for good laboratory practices and good clinical practices.

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Annexure 1: Preformed Questionnaire having question related to TORCH infection

Group A (Q. 1-4) Write full form of

Q. 1 TORCH; Q. 2 TORCHS; Q. 3 TORCHES; Q. 4 CHEAPTORCH

Group B (Q. 5-8) Write brief clinical manifestation of congenital

Q. 5 Toxoplasma; Q. 6 Rubella; Q. 7 CMV; Q. 8 Hereps

Group C (Q. 9-12) Indication of torch test i.e., When torch test should be requested

Q. 9 What test profile will you recommended in a pregnant (three month) and non-pregnant female with BOH?

Q. 10 What test profile will you recommend in a > six-month-old infant with congential anomaly?

Q. 11 When TORCH serology should not be recommend?

Q. 12 In addition to TORCH serology results, what confirmatory test you like to do?

Group D (Q. 13-30) Give result interpretation of following TORCH profile that is The resident should answer that if they receive result of TORCH test as TOXO IgG-, TOXO IgM+ than what they understand for example the answers are following

Group D (Q. 13-30) Give result interpretation of following TORCH profile.			
Q. No.	**TOXO IgG**	**TOXO IgM**	**Result Interpreation**
13	-	-	The patients is negative for *Toxoplasma* infection.
14	-	+/-	The patient may have fresh *Toxoplasma* infection.
15	-	+	Patient is having fresh *Toxoplasma* infection.
16	+/-	-	Patient may have previous infection
17	+/-	+/-	Patient may have fresh or previous infection
18	+/-	+	Patient is having fresh infection and might have previous infection
19	+	-	Patient is not having fresh infection but had it previously
20	+	+/-	Patient might have fresh infection but had it previously
21	+	+	Patient is having fresh *Toxoplasma* infection with longer duration of present infection or he/she had it previously
	Rubella IgG	**Rubella IgM**	
22	-	+	Patient is having fresh infection
23	+	-	Patient is not having fresh infection but had it previously
24	+	+	Patient is having fresh infection with longer duration of present infection or he/she had it previously
	CMV IgG	**CMV IgM**	
25	+	-	Patient is not having fresh infection but had it previously
26	+	+	Patient is having fresh infection with longer duration of present infection or he/she had it previously
27	-	+	Patient is having fresh infection
	HERPES IgG	**HERPES IgM**	
28	+	-	Patient is not having fresh infection but had it previously
29	+	+	Patient is having fresh infection with longer duration of present infection or he/she had it previously
30	-	+	Patient is having fresh infection