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EVALUATION OF THE APPLICABILITY OF LIGHT'S CRITERIA FOR DIFFERENTIATION OF TRANSUDATES FROM EXUDATES ACROSS DIFFERENT SEROUS FLUIDS

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ABSTRACT:

INTRODUCTION: *Serous fluids like pericardial, pleural and ascitic fluids are frequently submitted for pathological evaluation. The differentiation of these fluids into transudates and exudates is the prime aim of the evaluation as this determines the patients' further management. Light's criteria, proposed about 50 years ago, utilize various biochemical parameters for this differentiation and are the most widely used criteria.*

MATERIAL & METHODS: *This study was carried-out in Pathology department of Punjab Institute of Cardiology, Lahore. 60 serous fluid samples, including pericardial, pleural and ascitic fluids were analyzed routinely and classified into transudates and exudates applying Light's criteria. The proportion of transudates and exudates were compared amongst different fluids by applying chi-square test, keeping level of significance at p-value <0.05. Cytological examination was reported according to the International System for Reporting Serous Fluid Cytopathology.*

RESULTS: *Most of the fluids, i.e., 44 out of 60 were exudates. This trend was most pronounced for pericardial fluids where 29 out of 31 were exudates. 13 pleural fluids out of 23 were exudative while only 2 out of 6 ascitic fluids were exudative. On cytological examination, 55 fluids were negative for malignant cells, 2 fluids harbored atypical cells and 3 were positive for malignant cells. Careful gross examination of fluids furnished vital information in many cases.*

CONCLUSION: *Light's criteria may not be equally applicable across all types of fluids. In our study it had a high sensitivity but low specificity for pericardial exudates. Hence, modification of the criteria may be required to enhance its validity. Careful gross and cytological examination may provide additional invaluable information that could significantly impact management strategies.*

KEY WORDS: *Pleural fluid, pericardial fluid, light's criteria, transudate, exudate.*

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INTRODUCTION

Serous effusions like pleural effusion, pericardial effusion and peritoneal effusion, also referred to as ascites, are frequently encountered in clinical practice. The collected fluid is often drained and sent for laboratory examination. The process of drainage of pleural, pericardial and ascitic fluids is referred to as thoracocentesis, pericardiocentesis and paracentesis respectively.[1,2] These fluids are then submitted to a pathology laboratory for analysis. The main purpose of this is to dichotomize the fluids into transudates or exudates and to identify any atypical, suspicious, or malignant cells. These distinctions help in the further management of the patient.

The criteria of differentiation between transudates and exudates is an area of active debate. The paper by Light et al was the first to offer crisp and clear biochemical cut offs to differentiate between the two categories (Fig 1). Since then, it has been the mainstay of pathological analysis of fluids. Though originally described for pleural effusions, Light's criteria has been applied to pericardial as well as peritoneal effusions with variable reported credibility.[3]

The major objection to this criteria is that it has a high sensitivity but low specificity. In simple terms, more transudates would be classified as exudates than vice versa. In fact, numerous workers have proposed modifications to the criteria especially for pericardial and ascitic fluids.[1,4]

As already stated, the distinction of any aspirated fluid as a transudate or an exudate helps to determine the further management of the patient. The common causes of transudative effusions are congestive heart failure, cirrhosis, hypoalbuminemia, nephrotic syndrome, and radiotherapy. On the other hand, exudates commonly result from infections, cancer, tuberculosis, trauma, and pulmonary embolism.[1,5] There are fundamental pathophysiological differences in the mechanism of production of transudates and exudates. In the formation of transudates, the accumulation of fluid occurs in the extravascular compartment is due to an imbalance of Starling's forces, i.e., imbalance of oncotic and hydrostatic pressures; the permeability of vessel walls is essentially unchanged. While exudates are produced under inflammatory conditions which result in increased permeability of vessel walls.[5-7]

This study was designed to find the relative proportions of transudates and exudates in pleural, pericardial and ascitic fluids received in our laboratory, as well as to evaluate the efficacy of Light's criteria in classifying these fluids into transudates and exudates.[3]

MATERIALS AND METHODS:

This study was carried-out in Pathology department of Punjab Institute of Cardiology, Lahore. Sixty-three serous fluid samples, including pericardial, pleural and ascitic fluids, were received in our laboratory during the period of study. Three fluids that were necrotic and purulent were excluded because biochemical values of such fluids cannot be reliably determined. The remaining sixty samples were analyzed, and the results recorded.

After assessing the gross characters of the fluids like the color, volume, turbidity, sediment and any coagulum, the fluids were subjected to biochemical evaluation. This included the determination of their glucose, protein and LDH levels. The white and red blood cell counts were recorded, and then differential counts were determined by cytological examination of stained smears. This examination also included evaluation of other features like mesothelial cell characters as well as atypical, suspicious, or malignant cells if any. The newly described International System for Reporting Serous Fluid Cytopathology was followed for reporting.[8,9]

The data was entered into Microsoft Forms from where Microsoft Excel sheets were created and analyzed. The fluids were divided into transudates or exudates using Light's criteria as described above. The criteria requires simultaneously drawn blood samples as well. Where these were not available, cutoff values of 3 gm/dl for fluid protein level and 200 U/lit for fluid LDH levels were used as described in literature.[1,5,10,11]

The difference in proportion of transudates and exudate between different fluids was analyzed by chi square test. Results were considered significant if p-value was <0.05.

RESULTS:

The present study included fluids from 60 patients of whom 31 were males and 29 females. The commonest age group was 40-49 years (Figure 1). The majority of fluids were pericardial (31), followed by pleural (23) and ascitic fluids (6).

Careful gross examination of fluids revealed vital information in most cases (Figure 2). Transparent, pale colored fluids with low turbidity and no sediment were discovered to have biochemical values favoring transudates. On the other hand, turbid fluids with sediments, or those showing admixture with blood fell into the category of exudates following the criteria described.

Most fluids were exudates, as is seen in Figure

Table 1: Light's criteria for differentiating transudates and exudates[3]
An exudate meets one or more of the following criteria while a transudate meets none:
Fluid protein to serum protein ratio > 0.5
Fluid LDH to serum LDH ratio > 0.6
Fluid LDH level more than 2/3 of the upper normal limit of serum LDH

Table 2: Comparison or proportions of transudates vs exudates between different fluids		
Fluids being compared	***p*-value**	**Significance or otherwise at p<0.05**
Pericardial vs pleural fluids	0.001211	Highly significant
Pericardial vs ascitic fluids	0.00025	Highly significant
Pleural vs ascitic fluids	0.311405	Not significant

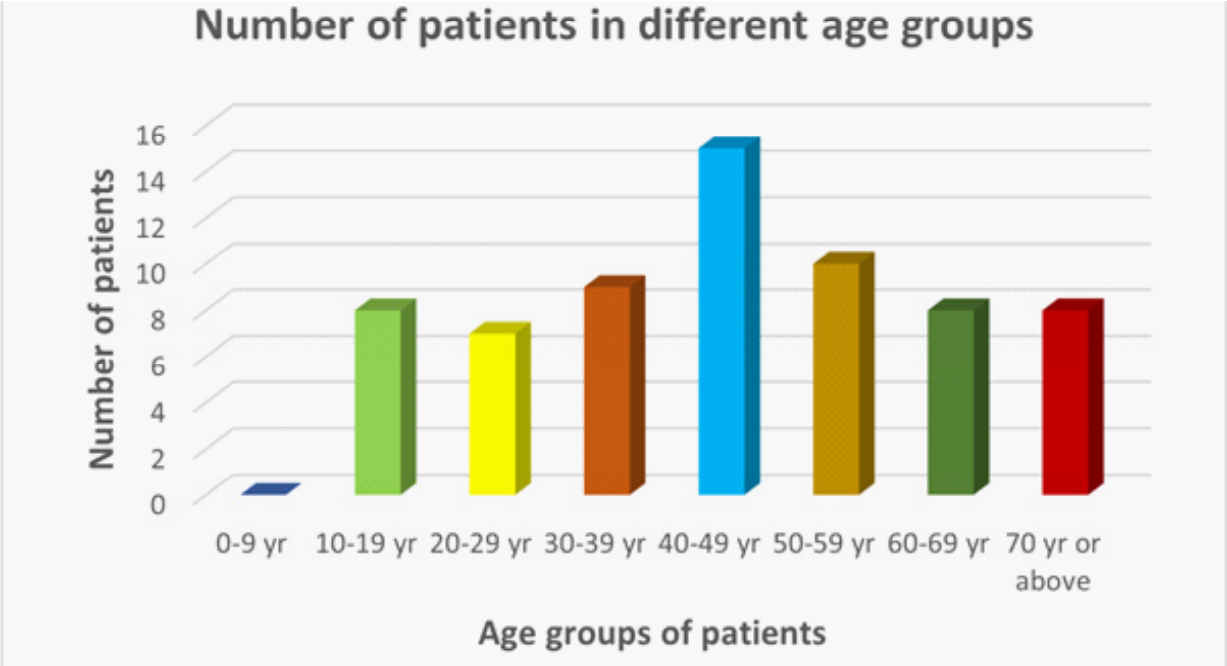

Figure 1: Serous effusions were most commonly seen in the 40 to 49-year age group.

3. This was especially true for pericardial fluids where 29 out of 31 samples were exudates. As for pleural fluids, 13 out of 23 fluids were exudates. A total of 6 ascitic fluids were received out of which only 2 were exudates. Overall, 44 out of 60 fluids were exudates.

The proportion of exudates out of the total fluids in the three categories were compared using chi square test. The results are given in Table 2. The difference in proportions of transudates vs exudates was highly significant when pericardial fluids were compared with either pleural or ascitic fluids. The difference between these proportions did not reach statistical significance when pleural and ascitic fluids were compared.

On cytological examination, 55 fluids were negative for malignant cells, 2 had atypical cells and 3 were positive for malignant cells. All 3 cases with malignant cells were known cases of malignancy. One was being treated for carcinoma breast, another for carcinoma lung, while the third was diagnosed with carcinoma breast 4 years ago. This patient had undergone surgery as well as chemotherapy at the time and was considered disease free at the time of current presentation. Development of pericardial effusion as well as discovery of malignant cells was totally unexpected (Figure 4).

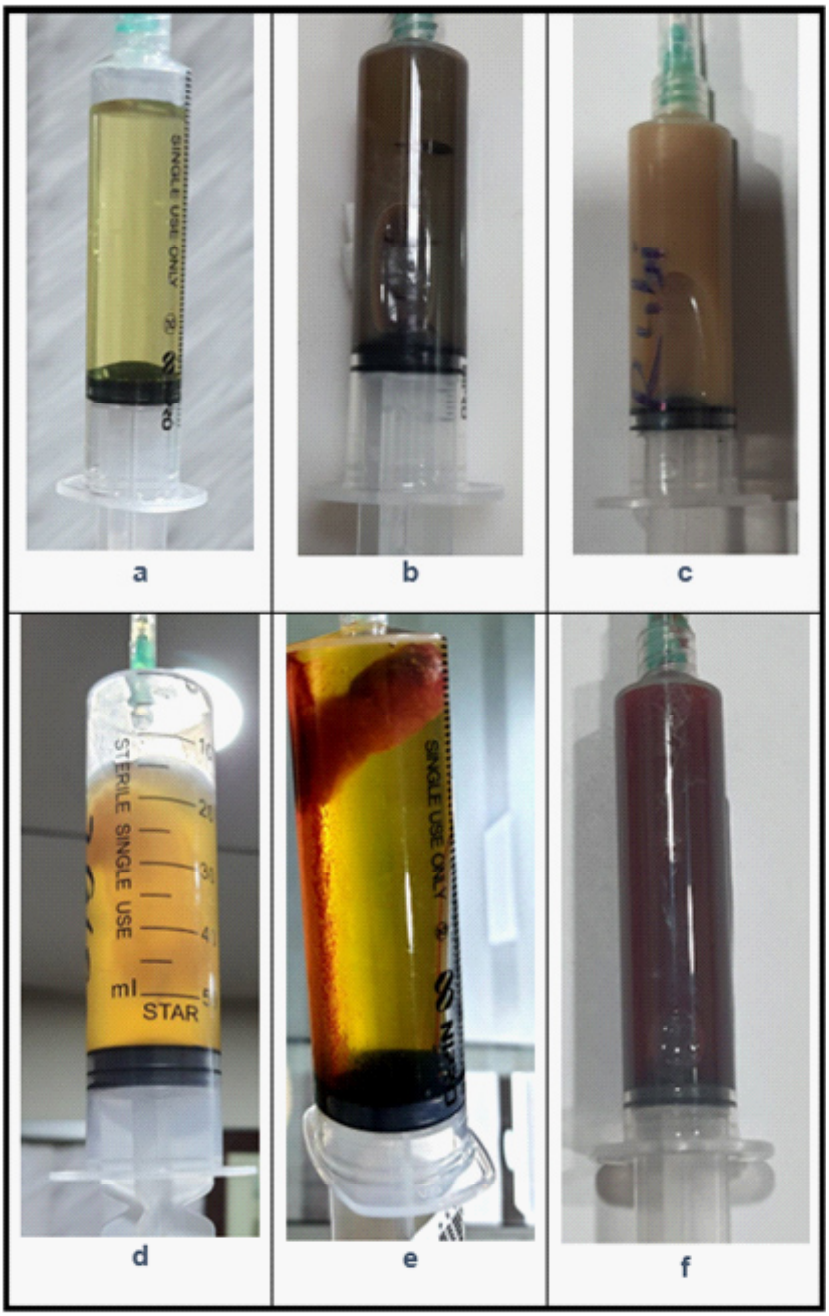

Figure 2: Gross examination of fluids can provide valuable information. a) This pale colored, transparent fluid is "clearly" a transudate. b) This sample with obvious turbidity had biochemical values of an exudate. c) A heavily turbid, purulent appearing sample which could not be included in the study as discussed in text. d) Close examination reveals a delicate "cobweb" coagulum. The pleural sample was taken from a tuberculous patient. e) This sample contains a clot. Since cells are likely to get entrapped in such clots, the cellular counts will be affected. Sending hemorrhagic samples in EDTA vials would prevent this. f) This pericardial fluid from a patient of carcinoma breast contains a heavy admixture of blood. This is going to alter the biochemical values as well as cell counts.

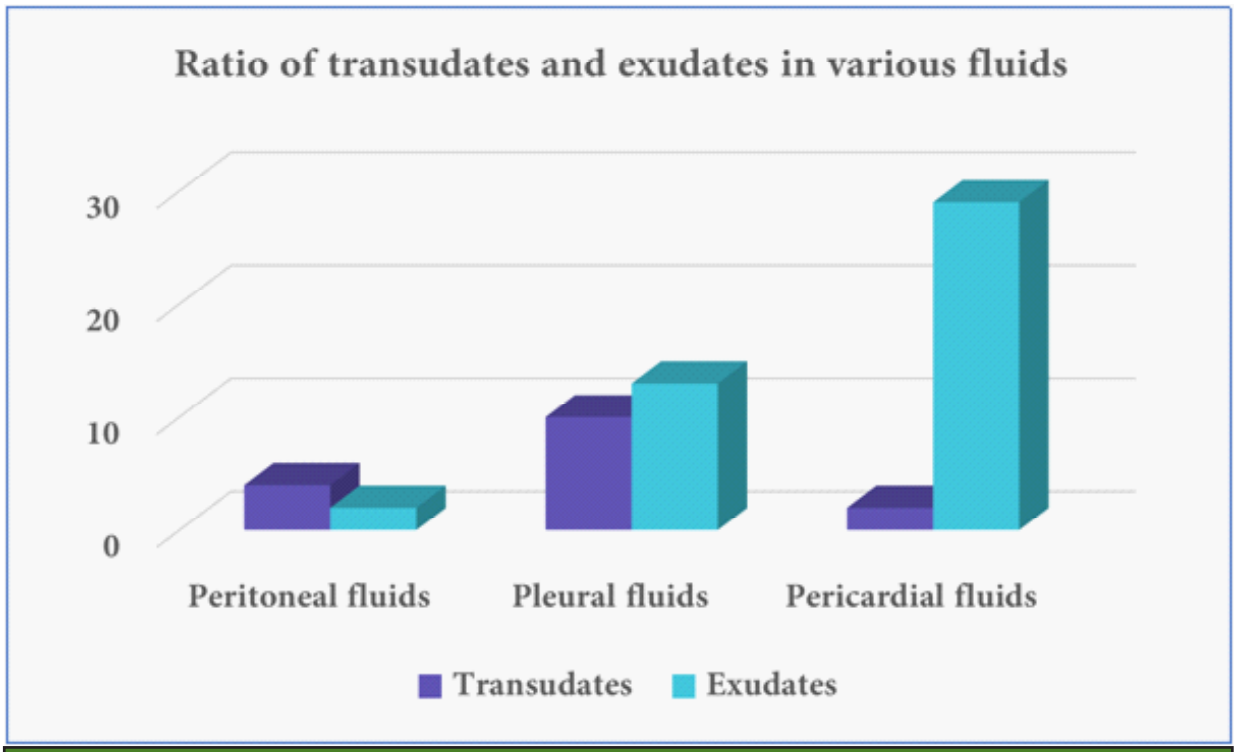

Figure 3: Bar chart showing the ratio of transudates to exudates in the three types of fluids.

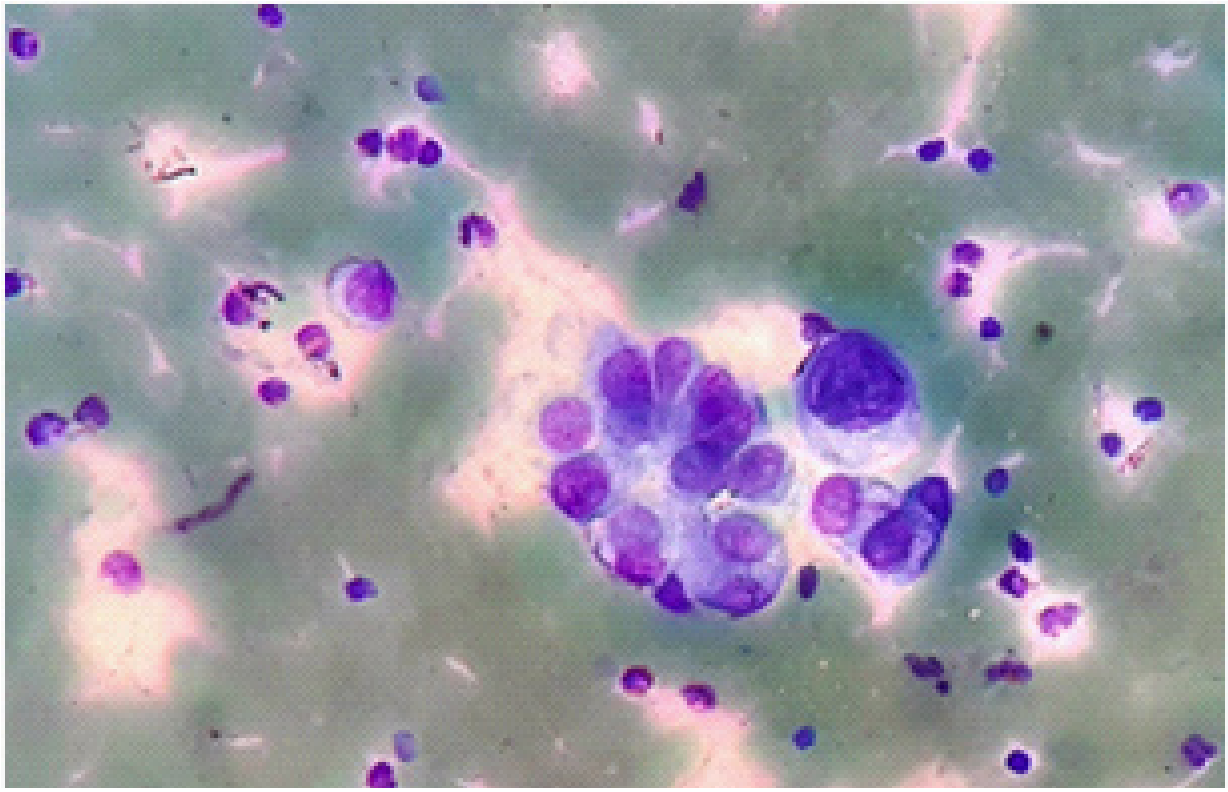

Fig 4: Photomicrograph showing a group of malignant cells in a pericardial fluid specimen. The 45-year-old patient was diagnosed with carcinoma breast four years ago.

DISCUSSION:

Serous fluid examination is aimed at determining the possible cause of the effusion and the prime objective is to determine whether the submitted fluid is a transudate or an exudate. In addition, findings like the number and type of inflammatory cells and presence or absence of atypical or malignant cells can shed additional light on the underlying cause of the effusion. Features of lesser significance may provide invaluable clues. Careful observation of fluid can reveal a cobweb coagulum, pointing to the possibility of tuberculosis (Figure 2). A low glucose level of <60 mg/dl, high WBC counts with neutrophilic predominance supports the suspicion of bacterial infection.[7] A lymphocytic predominance is seen in transudates, tuberculous exudates and in association with autoimmune diseases or lymphoid malignancies.[12,13]

The present study included fluids from 60 patients of whom 31 were males and 29 females. The difference between the two genders was not statistically significant. This is in keeping with findings of other studies.[2,8] The commonest age group was 40-49 years (Figure 1). This too closely matches the findings previously reported.[14] The majority of fluids were pericardial, followed by pleural and ascitic fluids (Figure 3). This may be explained considering that our hospital is primarily a cardiac hospital.

In the present study exudates far outnumbered the transudates. Similar findings have been reported previously, with exudates being 75-80% of the total.[15,16] In our study, this predominance of exudates was especially prominent for pericardial effusions; only 2 out of 31 pericardial fluids were transudates (Figure 3). Other studies have already reported similar findings. Ben-Horin et al reported that 118 out of 120 pericardial fluids included in their study were exudates.[17] Apparently, when it comes to pericardial exudates, the criteria has high sensitivity but low specificity. Therefore, this high proportion of exudates has prompted researchers to call for revised criteria for differentiation of pericardial fluids into transudates or exudates. It has been argued that Light's criteria were formulated keeping only pleural fluids in view. They need to be validated for fluids from other sources.[17-19] Findings of our study also support this view.

It was observed that a high number of fluids were hemorrhagic (Figure 2). In most cases this was probably caused by the trauma associated with the procedure. In a few cases, this admixture with blood was pronounced. This is obviously likely to influence biochemical values as well as cell counts.[6] So, both these parameters should be assessed cautiously in fluids that become markedly hemorrhagic. Occasionally fluids were seen to contain blood clots (Figure 2). A phenomenon with an even greater likelihood to warp values as cells would get trapped in the clot. One possible solution to the problem is to send markedly hemorrhagic smears in EDTA vials to prevent clotting.[20] Interpretation would become more meaningful if a concurrently drawn blood sample is also sent.[3] The differential leukocyte count ratios of the two specimens could shed additional light on whether the sample has neutrophilic or lymphocytic predominance.[21]

One apparently unsurmountable problem, faced universally, is the insufficient history and clinical data provided with effusion and other samples. In this day of advanced communications, this gap could easily be bridged if both the requesting and reporting sides are determined.[22]

Another predicament, commonly encountered, is degenerative changes in received samples. This happens when there is a lag between the times the sample is drawn and reported. While this may be inevitable in certain cases, every effort should be made to minimize it. If unavoidable, samples should be stored in a refrigerator till they can be processed.[20,23] Effusion samples like all other samples are precious and should be treated with utmost care (Figure 4). Deterioration due to high temperature is detrimental to almost all features and is commonly seen in a country with a hot climate like ours.[24] One thing to be kept in mind is that storage in a refrigerator can adversely affect culture of bacteria. So, a part of the sample should be kept at room temperature for culturing of bacteria.[25,26]

CONCLUSION AND RECOMMENDATIONS:

Differentiation of fluids into transudates or exudates is a prime aim of serous fluid analysis. The criterion for this differentiation is constantly evolving and is not necessarily the same for each type of fluid.

Effusion samples can provide invaluable information that can significantly impact management strategies. To optimize the furnished information each sample should be treated with utmost care at the point of care as well as in the laboratory. The following recommendations can help in deriving the maximum benefit for the patient:

- Each sample should be submitted with adequate history and clinical data.
- Two-way communication channels between

clinical and diagnostic sides should be ensured.
•In the case a delay is anticipated, a portion of the fluid should be kept refrigerated.
•Markedly hemorrhagic fluids should be submitted in EDTA vials to prevent clotting.

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