

**A CLINICOPATHOLOGICAL STUDY OF CERVICAL LYMPHADENOPATHY**Abhishek Maheshwari<sup>1</sup>, Rajesh Kumar Padhy<sup>2</sup>, Bijoy Kumar Dash<sup>3</sup>**HOW TO CITE THIS ARTICLE:**

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**ABSTRACT: BACKGROUND AND OBJECTIVE:** Cervical lymphadenopathy is the most common site of peripheral lymphadenopathy and is frequently encountered in otorhinolaryngology practice. Assessment and predicting its clinical behavior is not an easy task. Fine needle aspiration cytology (FNAC) is being routinely adopted as a special technique to diagnose the cause of lymphadenopathy. This study was undertaken to identify the clinic-demographic parameters in distribution of cases of cervical lymphadenopathy. FNAC was evaluated as a diagnostic tool by corroborating its results with histopathological examination of the excised lymph nodes. **MATERIAL AND METHODS:** This study was carried out at Hi-Tech Medical College and Hospital, Bhubaneswar, on 100 patients of cervical lymphadenopathy, over a period of two years. Along with detailed history, meticulous clinical examinations and investigations were performed. In all cases the diagnosis provided by FNAC and histopathology examination of the excised lymph node were correlated. **RESULTS:** Tuberculosis (45%) was the most common cause of cervical lymphadenopathy, followed by reactive (26%) and metastatic secondaries (21%) and lymphoma (8%). Maximum presentation was in 3<sup>rd</sup> decade (22%) and bilateral involvement was seen in 20% cases. Posterior triangle was the most common site involved (45%). Overall diagnostic accuracy of FNAC was 92%. **CONCLUSION:** Most common cause of cervical lymphadenopathy are tuberculosis, reactive lymphadenitis and metastatic secondaries. FNAC is a cheap, quick, readily available and dependable diagnostic modality and can be used as a first line investigatory tool in outdoor departments.

**KEYWORDS:** Cervical Lymphadenopathy, fine needle aspiration cytology, histopathological examination, tuberculosis.

**INTRODUCTION:** Lymphadenopathy is an abnormal increase in size and/or altered consistency of lymph nodes. It is a term synonymously used with "swollen/enlarged lymph nodes".<sup>1</sup> Cervical lymphadenopathy is a fairly common clinical entity that presents as a diagnostic challenge to the attending clinician. The underlying aetiological causes are numerous and diverse, but can broadly be considered to be reactive, infective or malignant in nature. Cervical lymphadenopathy can present as an isolated feature or as a part of generalized lymphadenopathy.<sup>2</sup>

Based on the duration, cervical lymphadenopathy is further classified into acute lymphadenopathy (2 weeks duration), subacute lymphadenopathy (2-6 weeks duration) and chronic lymphadenopathy (>6 weeks).<sup>3</sup> In paediatric age group, cervical lymphadenopathy is mostly due to pyogenic and granulomatous diseases where as in elderly, carcinoma of head and neck region are the most common causes. These cases of cervical lymphadenopathy are evaluated clinically, radiologically and pathologically (aspiration cytology and open biopsy). As compared to open biopsy, fine needle aspiration cytology (FNAC) has come up, as a parallel, but separate discipline for the diagnosis of cervical lymphadenopathy. Diagnosis is obtained quickly, complications are almost negligible and diagnostic accuracy is high.<sup>4</sup>

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The present study represents our quest to find out the epidemiological parameters pertaining to cervical lymphadenopathy and the role of FNAC as compared with open biopsy results.

**MATERIAL AND METHODS:** After approval from the institutional ethics committee, this study was carried out at Hi-Tech Medical College and Hospital, Bhubaneswar, over a period of two years. Out of all patients attending ENT outdoor 100 consecutive cases of cervical lymphadenopathy who gave their willful written informed consent, without age and sex bias were enrolled in this study.

A detailed history was taken and note was made regarding age, sex, duration of symptoms, constitutional symptoms and history of contact with tuberculosis patient. A complete physical examination was carried out. Importance was given to local examination in respect to site, size, number, unilateral/bilateral, consistency, mobility, matted/discrete and abscess/sinus. Patients were also examined for involvement of other (like inguinal and axillary) lymph nodes. Later the patients were subjected to following routine and special investigations. Routine investigations include, Hb percentage, total count, differential count, ESR, Chest X-ray. Special investigations include Mantoux test, Sputum for AFB, FNAC and open biopsy of the lymph node. The pathologists who performed histopathological examination (HPE) of biopsy specimens were unaware of the results of FNAC smears. Finally the results of FNAC and HPE were compared and sensitivity, specificity and diagnostic accuracy of FNAC was calculated.

All the patients confirmed as tubercular cervical lymphadenitis was put on short-term (DOTS) chemotherapy. Cases of reactive lymphadenopathy, lymphoma and metastatic secondaries were treated with the prevailing standard protocols. Surgery in addition to chemotherapy was reserved for situations like treatment of cold abscess and sinus, nodes that have not resolved with chemotherapy, large node, as part of neck clearance along with excision of primary tumor.

**OBSERVATIONS:** A total of 100 patients were evaluated as part of this study. The various causes of cervical lymphadenopathy were classified according to cytomorphological patterns and their frequency of occurrence in relation with different age and sex groups is shown in Table 1. Male predominance (54%) was noted and the maximum presentation was in 3<sup>rd</sup> decade (22%). Tuberculosis was the most common cause identified (45%), followed by reactive lymphadenitis (26%) and metastatic (21%).

Examination (Table 2) revealed that right side (47%) was more commonly affected than left side (33%) and bilateral involvement was seen in 2 cases (2%). The cervical lymph nodes were of less than 3cm size in 73% cases, 3-6 cm in 19% cases and more than 6 cm in 8% cases. Clinically the involved lymph nodes were firm in 65% cases, hard in 19% cases and soft in 16% cases. In 65% cases the lymph nodes were discrete and in 35% cases they were matted. Involved nodes were mobile in 80% cases and fixed in 20% cases. Disease process involved single lymph node group in 63% cases, two groups in 23% cases, whereas more than two groups were involved in 14% cases. It was observed that posterior triangle (level V) was the most common site of lymphadenopathy (45%), followed by upper jugular (level II) in 24% cases (Table 3). ESR was raised in 53% cases.

In case of tubercular lymphadenitis (Table 4) a history of exposure to a tuberculosis patient was present in 11 cases (24.44%). ESR was raised in 20 cases (44.44%), co-existing active lesions of tuberculosis were found in chest x-ray in 2 cases (4.44%). Mantoux test was positive in 33 cases (73.33%).

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The incidence of Hodgkins lymphoma and Non-Hodgkins lymphoma was observed in the ratio of 1.67:1. Primary site was identified in 14 cases (66.66%) of secondary metastatic deposits, while in remaining 7 cases (33.33%) it remained unknown. Oral cavity was the most common primary site, reported in 6 cases (42.86%), and was followed by larynx and thyroid in 3 cases (21.43%) and 2 cases (14.29%) respectively, (Table 5).

Finally the diagnosis provided by histopathological examination (biopsy) & cytological study (fnac) were correlated (Table 6). For FNAC an overall diagnostic accuracy of 92 % was noted. The sensitivity and specificity of FNAC, for diagnosing various lesions was calculated (Table 7)

**DISCUSSION:** Lymph nodes are considered to be the fortresses that aid immune defense.<sup>1</sup> Lymph nodes are encapsulated centres of antigen presentation and lymphocyte activation, differentiation and proliferation. They generate mature, antigen primed, B and T cells and filter particles, including microbes, from the lymph by the action of numerous phagocytic macrophages. These specialized immune cells called lymphocytes, detect and combat pathogens in the body. When inflamed, these nodes swell up, as they produce larger than normal quantities of lymphocytes.<sup>5</sup>

Howard and Lund have focused on an idea of having approximately 800 lymph nodes in the human body, out of which 300 nodes are located in the neck region alone.<sup>6</sup> Cervical lymphadenopathy is defined as cervical lymph nodal tissue measuring more than 1 cm in diameter.<sup>3</sup> It is a frequent finding amongst people of all age groups. Significant anxiety surrounds the finding of cervical lymphadenopathy amongst both, the patient as well as the attending clinician due to the concern regarding the underlying pathology. Till date, numerous studies have been undertaken on cervical lymphadenopathy, and perhaps cervical lymph nodes are the most frequently enlarged and biopsied nodes of all the peripheral lymph nodes.<sup>7</sup> Most cases can be diagnosed on the basis of a careful history and clinical examination. The causes include microbiological, haematological, neoplastic and connective tissue disorders.<sup>8</sup>

In the present study cervical lymphadenopathy was of non-neoplastic nature in 71 % cases, while the incidence of neoplastic type was 29%. This finding is consistent with the findings of Biswas G et al (2013)<sup>9</sup> who found an incidence of 71.6% and 28.3% respectively. The Observed male to female ratio was 1.17:1. This is in accordance with the observations of Pandav et al (2012)<sup>10</sup> and Adhikari et al (2011)<sup>11</sup>, who have also reported a male preponderance with a Male: Female ratio of 1.07:1 and 1.2:1 respectively. Cervical lymphadenopathy was most commonly seen in the 3<sup>rd</sup> decade with an incidence of 22%, followed closely by 4<sup>th</sup> decade (18%). This is in accordance with the findings of other researchers like Dukare et al (2014)<sup>12</sup> who reported maximum incidence (23.34%) in 3<sup>rd</sup> decade followed by 4<sup>th</sup> decade (15.49%) and Pandav et al (2012)<sup>10</sup> who have reported a maximum incidence in 3<sup>rd</sup> decade (21%).

In the present study tuberculosis was identified as the most common cause of cervical lymphadenopathy (45% cases), followed by reactive/ non-specific lymphadenopathy (26% cases). Similarly Vedi et al (2012)<sup>13</sup> reported Tuberculosis as the most common cause (50% cases) followed by reactive hyperplasia (30% cases). Unilateral involvement (80%) is more commonly noted than bilateral involvement (20%). It was also seen that right side (47%) was more commonly affected than the left side (33%). Similar results have been highlighted by other researchers. Vedi et al (2012)<sup>13</sup> reported unilateral (right side – 42.85% and left side – 35.71%) and bilateral involvement in 83.56% and 21.42% cases. Baskota et al (2004)<sup>14</sup> observed unilateral and bilateral disease in 83% and 17% cases respectively.

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In the present study, 73% cases stood into < 3cm group, 19% cases into 3-6 cm group, while 8% in > 6 cm group. This is in accordance with the results of Vedi et al (2012)<sup>13</sup> who reported categorization of 75%, 21.42% and 3.57% cases and Chamyal and Sabarigrish (1987)<sup>15</sup> who also categorized 69.1%, 20.9% and 10% cases in the same fashion.

Most common site of cervical lymphadenopathy as observed in the present study was level V (45%), followed by level II (24%) and level I (14%). In cases of tubercular lymphadenitis, the most common site affected was posterior triangle, which is in accordance with the results of Ismail and Muhammad (2013)<sup>16</sup> 50%, Maharjan et al (2009)<sup>17</sup> 42% and Baskota et al (2004)<sup>14</sup> 51%. The finding of maximum involvement of level III cervical nodes in cases of metastatic lymphadenopathy is consistent with the observations of Biswas G et al (2013).<sup>9</sup> In cases of lymphoma, the most common site involved was level V (posterior triangle), which is in accordance with the result of study conducted by Sharma et al (1993).<sup>18</sup>

It was observed that the consistency of involved nodes was soft in 16% cases which is mainly benign, firm in 65% cases which is mainly tubercular and hard 19% cases which is mainly metastatic. This finding is in accordance with the results of Vedi et al (2012)<sup>13</sup> who found soft nodes in 18.5% cases, firm nodes in 68.57% cases and hard nodes is 12.85% cases. It was also observed that the lymph nodes in cases of Hodgkins lymphoma are firm and rubbery, which is consistent with the study of Jamal et al (2008).<sup>19</sup>

It was observed in the present study that 80% of the involved nodes were mobile, while only 20% were fixed to the surrounding structures. This finding is consistent with the findings of Chamyal and Sabarigrish (1997)<sup>15</sup> who have found mobile lymph nodes in 60% cases and fixed in 16.4% cases.

It was observed that the disease process involved a single group of lymph nodes in 63% patients, 2 groups in 23% and >2 groups in 14% patients. This finding is in accordance with the study of Ismail and Muhammad(2013)<sup>16</sup> who observed that a single group of lymph nodes was involved in 60% of patients, 2 groups in 27.3% and >2 groups in 12.7% of patients. The observed results are also consistent with the findings of Baskota et al (2004)<sup>14</sup> who found that a single group of lymph nodes was involved in 68% of patients, 2 groups in 29% and >2 groups in 13% of patients.

In the present study, out of 45 cases of tubercular lymphadenitis, only 2 cases (4.44%) had coexisting active tubercular lesions confirmed on chest x-rays. This finding is in accordance with the observations of Daudpota et al (2013)<sup>20</sup> and Magsi et al (2013)<sup>21</sup> who had reported coexisting active tubercular lesions in chest in 3.64% and 7.5% cases respectively. 11 cases (24.44%) had a history of contact with a tuberculosis patient. This observation is in accordance with the study of Ismail and Muhammad (2013)<sup>16</sup> who reported a history of contact with tuberculosis patient in 27.8% cases. Nodes were matted in 31 cases (68.89%) and discrete in 14 cases (31.11%). This finding is consistent with the observation of Ismail and Muhammad (2013)<sup>16</sup> and Sharma et al (1993)<sup>19</sup> who reported matted lymph nodes in 67.8% and 72 % cases respectively. 25 cases (44.44%) had elevated levels of erythrocyte sedimentation rate, while it was normal in 20 cases. This finding is in accordance with the observations of Ismail and Muhammad (2013)<sup>16</sup> who found raised levels of ESR in 60% cases. Mantoux test was positive in 33 cases (73.33%), while it was negative in 12 cases (26.67%). This observation is consistent with the studies of Shrestha et al (2010)<sup>22</sup> and Biswas and Begum (2007)<sup>23</sup> who reported mantoux positivity in 76.19% and 70% cases respectively.

In the present study it is observed that out of a total of 8 cases of lymphoma, Hodgkin's were 5 cases (62.5%) and Non-Hodgkin's were 3 cases (37.5%). Therefore the observed ratio of Hodgkins

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to Non-Hodgkin's lymphoma is 1.67:1. The findings observed are in accordance with the study of Vedi et al (2012)<sup>13</sup> who reported incidence of Hodgkin's to Non-Hodgkin's lymphoma in the ratio of 2:1.

In the present study, in cases of metastatic lymphadenopathy the primary site was identified in 14 cases (66.66%), while in remaining 7 cases (33.33%) the primary site could not be detected (Occult primary). This finding is in accordance with the study of Prasad & Mohan (2014)<sup>24</sup> and Tapparwal et al (2013)<sup>25</sup> who are reported to have identified the primary site in 62.63% and 69% cases respectively. Out of 14 cases in which the primary site was identified, tumours of squamous origin were 78.57% while of non-squamous origin were 21.43%. This observation is consistent with the findings of Afroz et al (2009)<sup>26</sup>, who reported the origin as squamous and non-squamous in 81.13% and 18.87% cases respectively. Amongst the tumours of squamous origin the primary site was distributed in oral cavity, larynx, nasopharynx and lung in 42.86% 21.43%, 7.14% and 7.14% cases respectively. This finding is consistent with observations of Prasad and Mohan (2014),<sup>24</sup> who reported the distribution in oral cavity and lungs in 48.75% and 8.4% cases respectively. In cases of tumours of non-squamous origin the primary site was in thyroid in 14.29% cases and in parotid in 7.14% cases. This observation is in accordance with study of Afroz et al (2009)<sup>26</sup> who reported a primary site in thyroid gland in 15.09% cases.

The overall diagnostic accuracy of FNAC in case of cervical lymphadenopathy observed in the present study was 92%. This finding is in accordance with the results of other researchers like Adhikari et al (2011)<sup>11</sup> and Biswas S et al (2014),<sup>27</sup> who have reported an overall diagnostic accuracy of 90.9% and 88.4%

The sensitivity & specificity of fnac in diagnosing tubercular cervical lymphadenopathy as found in the present study is 91.11% and 96.36%. This finding is in accordance with the results of Biswas S et al (2014)<sup>27</sup> who reported sensitivity & specificity of 86.36% and 100%. The result is also consistent with the observations of Shrestha et al (2010)<sup>22</sup> who reported a sensitivity & specificity of 85.71% and 94.82%.

The sensitivity & specificity of fnac in diagnosing reactive/nonspecific cervical lymphadenopathy as found in the present study is 89.66% and 95.96%. This finding is in accordance with the study of Qadri et al (2012),<sup>28</sup> who have reported a sensitivity of 86% and a specificity of 95.9% for reactive hyperplasia cases.

The sensitivity & specificity of fnac in diagnosing lymphoma in cervical lymphadenopathy as found in the present study is 75% and 100%. This finding is comparable with the observations of Singh et al (2013)<sup>29</sup> who have reported a sensitivity of 81.48% and a specificity of 99.3% in diagnosing lymphoma with FNAC.

The sensitivity & specificity of fnac in diagnosing metastatic/secondaries in cervical lymphadenopathy as found in the present study is 86.36% and 96.20%. This observation is comparable with the studies of Biswas S et al (2014)<sup>27</sup> who found a sensitivity and specificity of 100% and 96.15%.

The gold-standard procedure for the diagnosis of a neck mass is open biopsy of the mass with histological examination of the excised tissue.<sup>30</sup> However, open biopsy of a metastatic cervical mass prior to definitive treatment of the neck (usually by radical neck dissection) in patients with metastatic cervical carcinoma has been reported to lead to a higher incidences of wound complications, regional neck recurrence and distant metastases, than in patients who have no biopsy performed prior to definitive treatment.<sup>31</sup>



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**CONCLUSION:** Commonest cause of cervical lymphadenopathy is tuberculosis followed by reactive lymphadenitis and metastatic secondaries. FNAC is simple, safe, quick, cheap, acceptable yet accurate method of establishing the etiology in cases of cervical lymphadenopathy. Its overall correlation in comparison to histopathological study is very high. Improper diagnosis and unjust treatment may convert a potentially curable disease into an incurable one. Hence it is imperative to establish diagnosis as early as possible in the course of evaluation, in order to institute specific treatment, thereby limiting complications.

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AGE GROUP (YEARS)	FINAL DIAGNOSIS										TOTAL		
	NON-NEOPLASTIC				NEOPLASTIC								
	Tuberculosis		Reactive/ non-specific		Hodgkins Lymphoma		Non-Hodgkins Lymphoma		Metastatic Secondaries		Total		Percentage
	M	F	M	F	M	F	M	F	M	F	M	F	%
0-10	3	4	3	3	-	-	-	-	-	-	6	7	13
11-20	4	4	6	3	-	-	-	-	-	-	10	7	17
21-30	1	8	4	4	2	1	1	-	-	1	8	14	22
31-40	8	7	1	-	-	-	1	-	1	-	11	7	18
41-50	2	2	1	1	-	1	-	-	2	1	5	5	10
51-60	1	-	-	-	1	-	-	1	5	3	7	4	11
61-70	1	-	-	-	-	-	-	-	3	1	4	1	5
71-80	-	-	-	-	-	-	-	-	3	1	3	1	4
<b>TOTAL</b>	<b>20</b>	<b>25</b>	<b>15</b>	<b>11</b>	<b>3</b>	<b>2</b>	<b>2</b>	<b>1</b>	<b>14</b>	<b>7</b>	<b>54</b>	<b>46</b>	
	45		26		5		3		21		100		100
	71				29						100		

TABLE 1: Age and Sex distribution among various lesions

VARIABLE	CLASSIFICATION	BENIGN		MALIGNANT			TOTAL/ PERCENTAGE	
		TUBERCULAR	REACTIVE	HODKINS LYMPHOMA	NON- HODGKINS LYMPHOMA	METASTATIC SECONDARIES		
SIZE	<3CM	41	23	3	1	5	73	
	3-6CM	4	3	2	2	8	19	
	>6CM	-	-	-	-	8	8	
SIDE	U/L	R	24	9	2	1	11	47
		L	19	3	2	1	8	33
	B/L	2	14	1	1	2	20	
CONSISTENCY	SOFT	8	6	1	-	1	16	



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	FIRM	36	19	4	3	3	65
	HARD	1	1	-	-	17	19
FIXITY	MOBILE	42	25	5	3	5	80
	FIXED	3	1	-	-	16	20
NUMBER OF GROUPS INVOLVED	SINGLE	40	18	-	-	5	63
	TWO	3	5	2	1	12	23
	> TWO	2	3	3	2	4	14

**TABLE 2: Examination findings**

SITE	BENIGN		MALIGNANT			TOTAL
	TUBERCULAR	REACTIVE	HODKINS LYMPHOMA	NON-HODKINS LYMPHOMA	METASTATIC SECONDARIES	
LEVEL I	5	6	-	-	3	14
LEVEL II	10	10	1	-	3	24
LEVEL III	4	1	-	-	6	11
LEVEL IV	2	-	-	-	2	4
LEVEL V	24	9	4	3	5	45
LEVEL VI	-	-	-	-	2	2
TOTAL	45	26	5	3	21	100

**TABLE 3: SITE DISTRIBUTION OF AFFECTED LYMPH NODES**

	Variable	No. of Cases	Percentage
Chest X-Ray	Positive	2	4.44
	Negative	43	95.56
History Of Contact	Present	11	24.44
	Absent	34	75.56
Node Status	Discrete	14	31.11
	Matted	31	68.89
ESR Level	< 20 Mm	20	44.44
	>20 Mm	25	55.56
Mantoux Test	Positive	33	73.33
	Negative	12	26.67

**TABLE 4: TUBERCULAR LYMPHADENITIS**

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Primary site	Origin	Site	No. of cases	Percentage		
Known	Squamous cell origin	Oral cavity (Tongue/buccal mucosa/palate)	6 (2/3/1)	42.86	78.57	66.66
		Nasopharynx	1	7.14		
		Larynx (Supraglottis/ subglottis)	3 (2/1)	21.43		
		Lung	1	7.14		
	Non squamous cell origin	Thyroid	2	14.29	21.43	
		Parotid	1	7.14		
Unknown	-	-	7	100 N=14	33.33	
Total	-	-	21		100 N=21	

**TABLE 5: DISTRIBUTION OF PRIMARY SITE IN CASES OF METASTATIC SECONDARIES IN NECK**

FNAC DIAGNOSIS	NUMBER OF CASES (FNAC)	HISTOPATHOLOGICAL DIAGNOSIS					ACCURACY (%)
		TUBERCULOSIS	REACTIVE/ NON SPECIFIC	HODGKINS LYMPHOMA	NON-HODGKINS LYMPHOMA	/METASTATIC SECONDARIES	
TUBERCULOSIS	43	41	-	-	1	1	95.35
REACTIVE/ NON-SPECIFIC	29	1	26	1	-	1	89.66
HODGKINS LYMPHOMA	4	-	-	4	-	-	100
NON HODGKINS LYMPHOMA	2	-	-	-	2	-	100
METASTATIC SECONDARIES	22	3	-	-	-	19	86.36
<b>TOTAL</b>	<b>100</b>	<b>45</b>	<b>26</b>	<b>5</b>	<b>3</b>	<b>21</b>	<b>92</b>

**TABLE 6: CORRELATION OF HISTOPATHOLOGICAL (BIOPSY) DIAGNOSIS & CYTOLOGICAL (FNAC) DIAGNOSIS**

## ORIGINAL ARTICLE

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FNAC DIAGNOSIS	SENSITIVITY (%)	SPECIFICITY (%)
TUBERCULOSIS	91.11	96.36
REACTIVE/ NON-SPECIFIC	89.66	95.96
LYMPHOMA	75	100
METASTATIC SECONDARIES	86.36	96.20

**Table 7: SENSITIVITY AND SPECIFICITY OF FNAC**

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