

## ORIGINAL ARTICLE

# Pattern of skin diseases prompting biopsy before and during the COVID-19 pandemic in Yogyakarta, Indonesia

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### Abstract

**Introduction:** Less biopsies were expected when large scale social restrictions were enforced during COVID-19 pandemic. **Aim:** To compare the skin diseases prompting biopsy before and during the COVID-19 pandemic. **Materials and Methods:** A retrospective study of skin diseases was performed; the skin problems were then grouped into major histopathological reactions. **Results:** A total of 229 biopsies were performed before the COVID-19 outbreak, whereas only 160 biopsies were done during the pandemic. Before versus during the outbreak, the proportion of major reactions were granulomatous 20.52% vs 21.88%, neoplasms 17.47% vs 20%, psoriasiform 14.85% vs 10%, vesiculobullous 9.61% vs 8.75%, others 10.92% vs 7.50%, interface dermatitis 6.99% vs 10%, vasculopathy 6.99% vs 5.63%, spongiotic 6.55% vs 8.13%, panniculitis 3.49% vs 3.75%, and superficial and deep dermal infiltrate 2.62% vs 4.38%. **Conclusion:** A decreased total number of patients prompting less biopsies were reported during the COVID-19 outbreak. However, the three largest percentages of major histopathological reactions were still similar, namely granulomatous, neoplasms, and psoriasiform.

**Keywords:** COVID-19, biopsy, dermatology, venereology

## INTRODUCTION

It is the main role of dermatologists and dermatopathologists to diagnose and manage patients presenting with primary skin diseases and skin manifestations of systemic problems. Skin biopsy is still an essential test to help dermatologists in formulating a precise diagnosis and treatment.<sup>1,2</sup>

The new Coronavirus Disease-2019 (COVID-19) initially found in Wuhan, China, created a global pandemic in 2020.<sup>3</sup> The first case in Indonesia was identified on March 2<sup>nd</sup>, 2020.<sup>4</sup> The fast-spreading COVID-19 cases and sky-rocketing number of deaths in Indonesia caused a decline in the number of people who visited hospitals since it is an airborne virus.<sup>5</sup> Therefore, this study aimed to describe the variety of conditions prompting skin biopsy in the first year of the COVID-19 pandemic by comparing with the previous year.

## METHODS

The study was conducted at Dr. Sardjito General Hospital, a tertiary hospital in the province of Daerah Istimewa Yogyakarta, Indonesia. A retrospective review of inpatient and outpatient dermatology consultations from April 2019-April 2021 was done. Data from the dermatology outpatient and inpatient summaries and pathology notes were collected. A final diagnosis was determined utilising both clinical and histopathological data, which were then grouped into 10 major histopathological reactions, namely interface dermatitis, psoriasiform, spongiotic, vesiculobullous, vasculopathy, granulomatous, superficial and deep dermal infiltrate, panniculitis, neoplasms, and "other". The ethical clearance (KE/0554/05/2021) for this study was obtained from the Medical and Health Research Ethics Committee of the Faculty of Medicine, Public Health and

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Nursing, Universitas Gadjah Mada, Yogyakarta, Indonesia. The total number of skin biopsies for each type of skin disorder were interface dermatitis 32 cases, spongiotic dermatitis 28 cases, psoriasiform 50 cases, vesicobullous 36 cases, vasculopathy 25 cases, panniculitis 14 cases, superficial and deep dermal infiltrate 13 cases, granulomatous 82 cases, neoplasms 72 cases, and others 37 cases.

## RESULTS

Between April 2019 and March 2020 (before the COVID-19 outbreak), our dermatology department performed 229 biopsies, while between April 2020 and March 2021 (during the COVID-19 outbreak), we completed 160 biopsies, with a 30.13% reduction and a significant difference ( $p=0.00$ ).

Of the 229 biopsies performed one year before the beginning of the COVID-19 pandemic, 54.59% were female patients, and 45.41% were male patients (Figure 1a). The mean age of the patient was 39.54 years old, ranging from newborn to 78 years old, with the highest percentage of age prompting biopsies was the third decade (21-30 years old) (Figure 1b). Biopsies with granulomatous as the major histopathologic reaction had the largest proportion with 20.52%, followed by neoplasms (17.47%) (Figure 1d). The highest percentage for each of the histopathology reactions were lupus erythematosus (62.50% for interface dermatitis), seborrheic dermatitis (40.00%, spongiotic), psoriasis (82.35%, psoriasiform), pemphigus vulgaris (31.82%, vesiculobullous), Henoch-Schonlein purpura (31.25%, vasculopathy), erythema nodosum (50%, panniculitis), leprosy (74.47%, granulomatous), and intradermal nevi (22.50%, neoplasms) (Table 1). Four patients required second biopsies to investigate the effect of the therapy for lupus vulgaris, chromoblastomycosis, psoriasis, and actinomycetoma.

On the other hand, of the 160 biopsies done one year after the start of the COVID-19 pandemic, 55% were female patients, and 45% were male patients (Figure 1a). The mean of the patients' age was 36.92 years old, ranging from newborn to 82 years old. The highest percentage of patients requiring biopsies during this pandemic period was 21-30 years old group (Figure 1b). During the first two months after the beginning of the outbreak, the dermatology and venereology department only performed three biopsies in April 2020 and two biopsies

in May 2020 (Figure 1c). The largest proportion of the major histopathological reactions were granulomatous (21.88%), neoplasms (20%), psoriasiform and interface dermatitis (both 10%). The highest proportion for diseases in each group were lupus erythematosus (43.75%, interface dermatitis), psoriasis (87.50%, spongiotic), bullous pemphigoid (42.86%, vesiculobullous), leprosy (65.71%, granulomatous) (Table 1). Three patients underwent two biopsies to investigate the course of psoriasis after therapy was given for 6 months and one patient for chromoblastomycosis.

## DISCUSSION

Histopathological results from biopsy are still the gold standard to diagnose skin diseases. Interpreting histopathological features from skin specimens consists of several steps. Here we presented a comprehensive review of primary dermatological problems and cutaneous manifestations of systemic diseases requiring biopsies before and during the COVID-19 pandemic which were grouped into the major histopathological reactions. Comparing before and during the pandemic, a thirty percent (30%) decrease of biopsies was observed during this time, with similar proportion of patient gender, from 229 biopsies to only 160 biopsies.

Several major histopathological reactions had similar percentages before and during the pandemic, and both groups had the same three largest proportion, namely granulomatous, neoplasms, and psoriasiform. The proportion of granulomatous reaction, with chronic granulomatous inflammation as the major features, was increased compared to before the outbreak, in addition, neoplasms was also increased. Spongiotic reaction showed an increased percentage during the pandemic. This is possibly due to the usage of hand sanitiser and gloves as preventive hygiene measures, which could cause contact dermatitis.<sup>6</sup> This could also possibly cause higher biopsy cases of contact dermatitis cases compared to atopic dermatitis cases during the pandemic. The skin condition due to the hand hygiene protocol could be prevented by educating the patients.<sup>7,8</sup> A previous studies reported that the most frequent major histopathological reactions in a tertiary care center in the United States were vasculopathy, interface dermatitis, and infectious disease.<sup>2</sup> In this study, both before and during the pandemic, the most frequent major histopathological reaction was granulomatous. Indonesia, Brazil,

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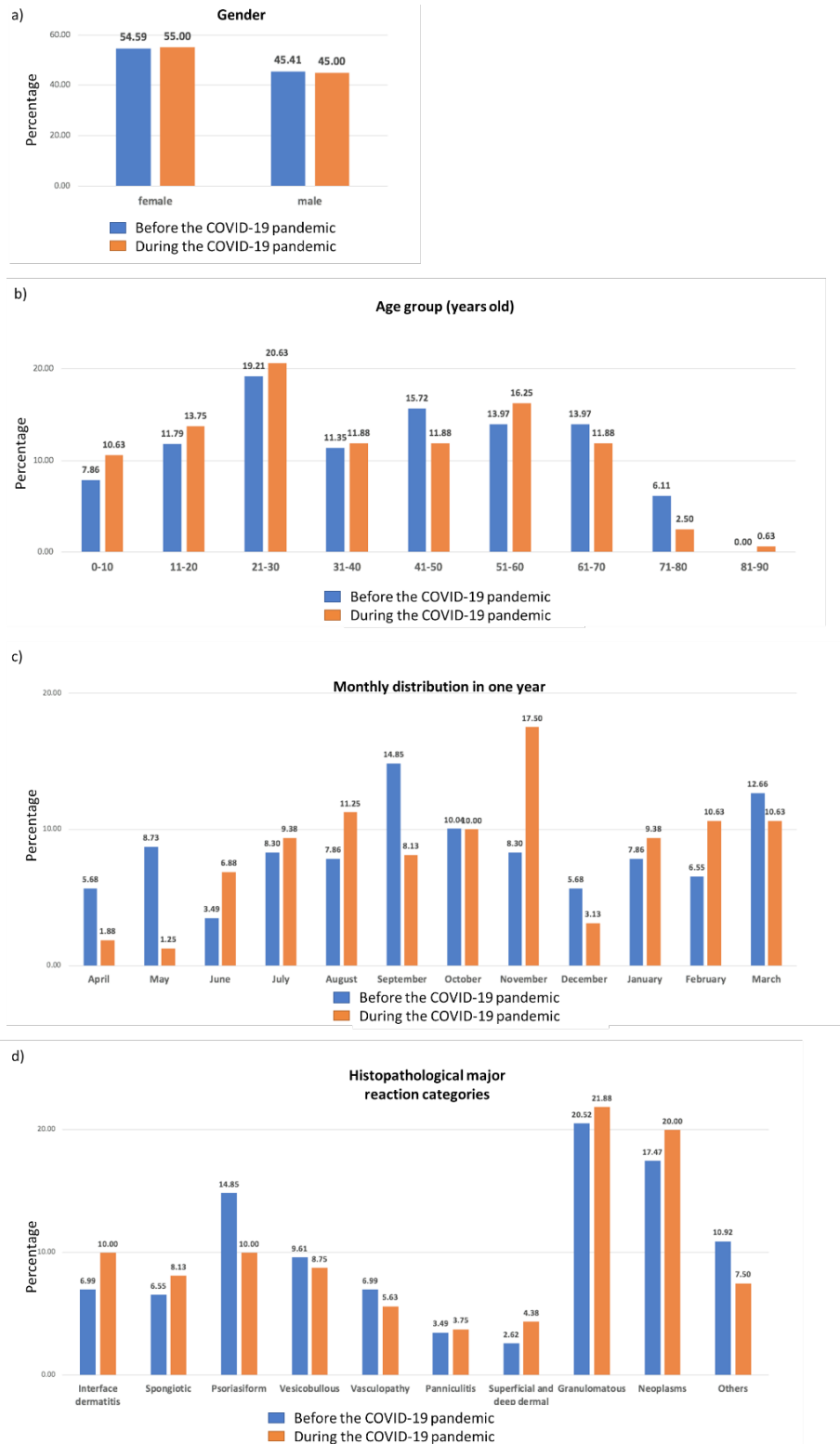


FIG. 1. a) Gender of patients in dermatology outpatient and inpatient clinics prompting biopsies in the Dr. Sardjito Hospital, Yogyakarta, Indonesia one year before and during the COVID-19 pandemic (percentage). b) Age of patients in dermatology outpatient and inpatient clinics prompting biopsies in the Dr. Sardjito Hospital, Yogyakarta, Indonesia one year before and during the COVID-19 pandemic (percentage). c) Monthly distribution of patients prompting biopsies in the Dr. Sardjito Hospital, Yogyakarta, Indonesia one year before and during the COVID-19 pandemic (percentage). d) Histopathological major reaction categories of biopsies performed by dermatologists in the Dr. Sardjito Hospital, Yogyakarta, Indonesia one year before and during the COVID-19 pandemic (percentage).

**Table 1: Diagnoses of patient biopsies by dermatologists in the Dr. Sardjito Hospital, Yogyakarta, Indonesia one year before and during the COVID-19 pandemic**

	Total number of patients before the COVID-19 pandemic	% before the COVID-19 pandemic	Total number of patients during the COVID-19 pandemic	% during the COVID-19 pandemic
<b><i>Interface dermatitis</i></b>	<b>16</b>	<b>6.99</b>	<b>16</b>	<b>10.00</b>
<i>Lupus erythematosus</i>	10	62.50	7	43.75
<i>Lichen sclerosus</i>	1	6.25	0	0.00
<i>Lichen planus</i>	0	0.00	2	12.50
<i>Drug eruption</i>	0	0.00	2	12.50
<i>Pityriasis lichenoides et varioliformis acuta (PLEVA)</i>	0	0.00	1	6.25
<i>Dermatomyositis</i>	3	18.75	1	6.25
<i>Radiation dermatitis</i>	0	0.00	1	6.25
<i>Erythema multiforme</i>	1	6.25	0	0.00
<i>Pityriasis lichenoides chronica (PLC)</i>	0	0.00	1	6.25
<i>Non-specific interface dermatitis</i>	1	6.25	1	6.25
<b><i>Spongiotic</i></b>	<b>15</b>	<b>6.55</b>	<b>13</b>	<b>8.13</b>
<i>Contact dermatitis</i>	2	13.33	3	23.08
<i>Atopic dermatitis</i>	1	6.67	2	15.38
<i>Seborrheic dermatitis</i>	6	40.00	3	23.08
<i>Pityriasis alba</i>	1	6.67	0	0.00
<i>Insect bite</i>	2	13.33	0	0.00
<i>Hyper IgE syndrome</i>	0	0.00	1	7.69
<i>Drug Rash with Eosinophilia and Systemic Symptoms (DRESS)</i>	0	0.00	1	7.69
<i>Papular pruritic eruption (PPE)</i>	1	6.67	0	0.00
<i>Pityriasis rosea</i>	2	13.33	2	15.38
<i>Non-specific spongiotic dermatitis</i>	0	0.00	1	7.69
<b><i>Psoriasiform</i></b>	<b>34</b>	<b>14.85</b>	<b>16</b>	<b>10.00</b>
<i>Psoriasis</i>	28	82.35	14	87.50
<i>Secondary syphilis</i>	2	5.88	0	0.00
<i>Erythroderma</i>	2	5.88	2	12.50
<i>Lichen simplex chronicus</i>	1	2.94	0	0.00
<i>Congenital ichthyosiform erythroderma</i>	1	2.94	0	0.00

<b>Vesicobullous</b>	<b>22</b>	<b>9.61</b>	<b>14</b>	<b>8.75</b>
<i>Bullous pemphigoid</i>	5	22.73	6	42.86
<i>Chronic bullous disease of the childhood</i>	1	4.55	0	0.00
<i>Pemphigus vulgaris</i>	7	31.82	1	7.14
<i>Pemphigus foliaceus</i>	3	13.64	2	14.29
<i>Pemphigus erythematosus</i>	1	4.55	0	
<i>Dermatitis herpetiformis</i>	1	4.55	0	0.00
<i>Bullous impetigo</i>	1	4.55	0	0.00
<i>Epidermolysis bullosa acquisita</i>	3	13.64	2	14.29
<i>Linear IgA dermatosis</i>	0	0.00	1	7.14
<i>Bullous systemic lupus erythematosus</i>	0	0.00	1	7.14
<i>Acute generalized exanthematous pustulosis (AGEP)</i>	0	0.00	1	7.14
<b>Vasculopathy</b>	<b>16</b>	<b>6.99</b>	<b>9</b>	<b>5.63</b>
<i>Erythema annulare centrifugum</i>	2	12.50	2	22.22
<i>Urticaria</i>	1	6.25	1	11.11
<i>Henoch–Schonlein purpura (HSP)</i>	5	31.25	0	0.00
<i>Pigmented purpuric dermatosis</i>	1	6.25	0	0.00
<i>Pyoderma gangrenosum</i>	2	12.50	2	22.22
<i>Polyarteritis nodosa</i>	1	6.25	0	0.00
<i>Livedoid vasculitis</i>	0	0.00	1	11.11
<i>Leukocytoclastic vasculitis</i>	1	6.25	0	0.00
<i>Lupus vasculopathy</i>	1	6.25	1	11.11
<i>Non-specific vasculopathy</i>	2	12.50	2	22.22
<b>Panniculitis</b>	<b>8</b>	<b>3.49</b>	<b>6</b>	<b>3.75</b>
<i>Erythema nodosum</i>	4	50.00	2	33.33
<i>Erythema induratum</i>	1	12.50	1	16.67
<i>Lupus panniculitis</i>	1	12.50	2	33.33
<i>Non-specific panniculitis</i>	2	25.00	1	16.67
<b>Superficial and deep dermal infiltrate</b>	<b>6</b>	<b>2.62</b>	<b>7</b>	<b>4.38</b>
<i>Langerhans cells histiocytosis</i>	2	33.33	2	28.57
<i>Cutaneous mastocytosis</i>	1	16.67	0	0.00
<i>Leukemia cutis</i>	0	0.00	1	14.29
<i>Cellulitis</i>	0	0.00	1	14.29
<i>B-cell lymphoma</i>	0	0.00	1	14.29

<i>T-cell lymphoma</i>	2	33.33	1	14.29
<i>Non-Hodgkin lymphoma</i>	0	0.00	1	14.29
<i>Non-specific infiltrate</i>	1	16.67	0	0.00
<b><i>Granulomatous</i></b>	<b>47</b>	<b>20.52</b>	<b>35</b>	<b>21.88</b>
<i>Leprosy</i>	35	74.47	23	65.71
<i>Chromoblastomycosis</i>	3	6.38	1	2.86
<i>Actinomycetoma</i>	2	4.26	1	2.86
<i>Sporotrichosis</i>	1	2.13	2	5.71
<i>Lupus granulomatous</i>	1	2.13	0	0.00
<i>Eumycetoma</i>	0	0.00	3	8.57
<i>Pyogenic granuloma</i>	0	0.00	2	5.71
<i>Non-specific granulomatous dermatitis</i>	5	10.64	3	8.57
<b><i>Neoplasms</i></b>	<b>40</b>	<b>17.47</b>	<b>32</b>	<b>20.00</b>
<i>Pseudoepitheliomatous hyperplasia</i>	1	2.50	0	0.00
<i>Intradermal nevus</i>	9	22.50	4	12.50
<i>Nevus Becker</i>	1	2.50	2	6.25
<i>Neurofibroma</i>	1	2.50	4	12.50
<i>Prurigo nodularis</i>	3	7.50	2	6.25
<i>Basal cell carcinoma</i>	4	10.00	2	6.25
<i>Nevus lipomatosis</i>	3	7.50	0	0.00
<i>Nevus sebaceous</i>	1	2.50	0	0.00
<i>Papilloma</i>	2	5.00	1	3.13
<i>Trichoepithelioma</i>	1	2.50	0	0.00
<i>Ductal carcinoma metastases</i>	1	2.50	0	0.00
<i>Porocarcinoma</i>	1	2.50	0	0.00
<i>Nevus epidermal</i>	2	5.00	0	0.00
<i>Fibroepithelial polyp</i>	0	0.00	2	6.25
<i>Seborrheic keratosis</i>	5	12.50	2	6.25
<i>Junctional nevus</i>	0	0.00	2	6.25
<i>Verucca vulgaris</i>	0	0.00	1	3.13
<i>Verucca plana</i>	0	0.00	1	3.13
<i>Actinic keratosis</i>	0	0.00	1	3.13
<i>Capillary hemangioma</i>	0	0.00	1	3.13
<i>Nevus depigmentosus</i>	0	0.00	1	3.13
<i>Dermatofibrosarcoma</i>	0	0.00	1	3.13
<i>Epidermoid cyst</i>	1	2.50	1	3.13
<i>Metastasis from thyroid</i>	1	2.50	0	0.00

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<i>Lymphangioma circumscriptum</i>	0	0.00	1	3.13
<i>Endovascular papillary hemangio-endothelioma (Tumor Dabska)</i>	1	2.50	0	0.00
<i>Nostras verrucosa</i>	1	2.50	0	0.00
<i>Pigmented nevi</i>	1	2.50	0	0.00
<i>Lentigenous nevi</i>	0	0.00	1	3.13
<i>Angiokeratoma circumscriptum</i>	0	0.00	1	3.13
<i>Depigmented nevi</i>	0	0.00	1	3.13
<b>Others</b>	<b>25</b>	<b>10.92</b>	<b>12</b>	<b>7.50</b>
<i>Scleredema</i>	1	4.00	0	0.00
<i>Ichthyosis</i>	0	0.00	1	8.33
<i>Leukoderma</i>	1	4.00	0	0.00
<i>Lentigo</i>	2	8.00	0	0.00
<i>Atrophoderma</i>	2	8.00	0	0.00
<i>Thyroid dermatopathy</i>	1	4.00	0	0.00
<i>Androgenetic alopecia</i>	1	4.00	0	0.00
<i>Idiopathic guttate hypomelanosis</i>	1	4.00	0	0.00
<i>Epidermodysplasia verruciformis</i>	1	4.00	0	0.00
<i>Hyperpigmentation post inflammation</i>	2	8.00	2	16.67
<i>Incontinentia pigmenti</i>	1	4.00	0	0.00
<i>Acquired perforating dermatosis</i>	1	4.00	0	0.00
<i>Amyloidosis cutis</i>	1	4.00	0	0.00
<i>Ochronosis</i>	1	4.00	0	0.00
<i>Hypopigmentation post inflammation</i>	0	0.00	1	8.33
<i>Scleroderma</i>	3	12.00	2	16.67
<i>Keloid</i>	0	0.00	2	16.67
<i>Folliculitis</i>	0	0.00	1	8.33
<i>Idiopathic eruptive macular hyperpigmentation</i>	0	0.00	1	8.33
<i>Condyloma acuminata</i>	1	4.00	0	0.00
<i>Vitiligo</i>	2	8.00	0	0.00
<i>Morphea</i>	1	4.00	1	8.33
<i>Alopecia areata</i>	1	4.00	0	0.00
<i>Rosacea</i>	1	4.00	1	8.33
<b>TOTAL</b>	<b>289</b>	<b>100%</b>	<b>160</b>	<b>100%</b>

p= 0.00

and India contributed to 80% of new leprosy cases which showed granulomatous reaction in the skin biopsy.<sup>9</sup>

Both before and during the COVID-19 outbreak, several diseases still had the largest proportion for each major histopathological reaction, namely, lupus erythematosus for interface dermatitis, psoriasis for psoriasiform, and leprosy for granulomatous. The data showed that these diseases required biopsies for the accurate diagnosis, such as biopsy for leprosy was needed to determine the type of leprosy and whether the condition was accompanied with leprosy reaction. For psoriasis, biopsy was required to confirm the diagnosis before a certain treatment was given, whereas for lupus erythematosus, results from biopsy were able to present whether vasculopathy, panniculitis, or interface dermatitis reaction were present in the patients, and whether the condition was acute, sub-acute, or the chronic cutaneous type of lupus erythematosus.<sup>10,11</sup>

## CONCLUSION

In this study, we compared diagnoses of skin diseases prompting biopsy before and during the COVID-19 pandemic. There was a significant difference ( $p=0.00$ ) and a thirty percent (30%) decrease of biopsies performed during the outbreak compared to before the pandemic. The three largest proportions of major histopathological reaction of skin problem requiring biopsies remained the same, with granulomatous as the largest, neoplasms as the second, and psoriasiform as the third.

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*Authors' contribution:* Agnes Rosarina Prita Sari: Conceptual framework, Literature review, Data analysis, Reference analysis, Manuscript preparation. Sunardi Radiono: Literature review, Reference analysis, Hardyanto Soebono: Conceptual framework, Literature review. Paranita Ferronika: Data analysis, Reference analysis, Manuscript preparation.

*Conflict of interest:* The authors declared no conflict of interest.

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