# Single-breath diffusion capacity of the lung for carbon monoxide in chronic obstructive pulmonary disease

Waleed M. El-Sorougi[a], Maha M. Fathy[b]

**Background** Chronic obstructive pulmonary disease (COPD) is defined by progressive, irreversible airflow limitation and an inflammatory response of the lungs, usually to cigarette smoke. However, COPD is a heterogenous disease in terms of clinical, physiological, and pathological presentation. The pathological hallmarks of COPD are inflammation of the small airways (bronchiolitis) and destruction of lung parenchyma (emphysema). The functional consequence of these abnormalities is airflow limitation.

**Aim of work** The aim of the study was to measure diffusion capacity in different stages of COPD.

**Patients and methods** Sixty outpatients with COPD with mild to very severe obstruction were included in the study.

**Results** There was a statistically significant negative (inverse) correlation between TLCO%, TLCO/VA, $PCO_2$, and $HCO_3$ and there was a statistically significant positive (direct) correlation between TLCO%, TLCO/VA, $PO_2$, and arterial oxygen saturation. There was a statistically significant positive (direct) correlation between FVC%, FEV1%, FEF25%, FEF50%, FEF75%, TLCO%, and TLCO/VA.

**Conclusion** Reduced diffusion capacity of the lung for carbon monoxide plus airflow obstruction together identifies a group of individuals with significantly worse lung function.
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**Keywords:** arterial blood gases, chronic obstructive pulmonary disease, diffusion capacity of the lung for carbon monoxide, spirometry

[a]Department of Chest Medicine, Faculty of Medicine, Helwan University, Helwan, [b]Department of Chest Medicine, Faculty of Medicine, Beni-Suef University, Beni-Suef, Egypt

Correspondence to Waleed M. El-Sorougi, MD, 27 Omar Bakeer Street, Saint Fatima Sq., Heliopolis, Cairo 11361, Egypt; Tel: +20 100 123 2700; fax: +20 277 44055;
e-mail: waleed@sorougi.com

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## Introduction

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease with significant extrapulmonary effects that may contribute to severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles and gases. The chronic airflow limitation characteristic of COPD is caused by a mixture of small airway disease (obstructive bronchiolitis) and parenchymal destruction (emphysema), the relative contribution of which varies from person to person [1].

In general, if the carbon monoxide transfer coefficient is normal, severe emphysema is effectively excluded, but a normal value does not exclude milder disease. In practice, in symptomatic patients with airway obstruction, the test is of most value in helping to distinguish emphysema from asthma in which carbon monoxide transfer coefficient is usually not reduced [2].

The diffusion capacity of the lung for carbon monoxide (DLco) is a standard test in the pulmonary function laboratory. The DLco is used in the assessment of restrictive as well as obstructive pulmonary disease, and is an indicator of disease severity. In COPD and in diffuse parenchymal lung disease the DLco is a strong predictor of desaturation during exercise [3].

## Aim of work

The aim of the study was to measure diffusion capacity in different stages of COPD.

## Patients and methods

Sixty male patients with COPD were included in this study. Patient inclusion criteria included chronic heavy smoking, dyspnea that is progressive, usually worse with exercise, and persistent, chronic cough with chronic sputum production. Exclusion criteria included bronchial asthma, bronchiectasis, long-term oxygen therapy, and other comorbidities such as cardiac, renal, and hepatic disorders. The study protocol was approved by local ethical committee and informed consent was taken.

The sixty patients with COPD were diagnosed clinically and functionally with airflow limitation and were divided




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according to the Global Initiative for Chronic Obstructive Lung Disease classification [4].

Each patient was subjected to full history taking, full clinical examination, radiological examination (chest radiography, chest computed tomography), and arterial blood gases. Pulmonary function was assessed by standard spirometric techniques, according to American Thoracic Society criteria [5]. Measurements were obtained for forced vital capacity (FVC), forced expiratory volume in the first second ($FEV_1$), and the ratio between them, peak expiratory flow, forced expiratory flow (FEF)25%, FEF50%, and FEF75%.

Single-breath diffusion capacity was measured according to the European Respiratory Society and American Thoracic Society recommendations [6]. Inspiration gas contained 0.267% CO, 9.409% He, and rest air. Measured DLco is expressed as milliliters of gas standard temperature, pressure, and dry (STPD) per minute per unit of driving pressure in mmHg. The predicted DLco is calculated using appropriate software. Percent measured DLco of predicted DLco is used to compare different groups. The DLco/alveolar volume (VA) is derived by dividing the measured DLco by the measured VA.

### Statistical analysis

Results are presented as mean and SD. Significance was determined at the 5% level. Nonparametric data from the study groups were compared by Kruskal–Wallis test.

## Results

As regards transfer factor of the lung for carbon monoxide (TLCO%) and TLCO/VA, there was no statistically significant difference between mild and moderate COPD groups, which showed the statistically significant highest mean values. The very severe COPD group showed the statistically significant lowest mean value (Tables 1–3).

As regards the whole sample, there was a statistically significant positive (direct) correlation between FVC%, TLCO%, and TLCO/VA. A decrease in FVC% is associated with a decrease in TLCO% and TLCO/VA.

In patients with mild and moderate COPD, there was no statistically significant correlation between FVC% and diffusion capacity. In patients with very severe COPD, there was a statistically significant positive (direct) correlation between FVC% and TLCO% (Table 4).

As regards the whole sample, there was a statistically significant positive (direct) correlation between FEV1%, TLCO%, and TLCO/VA. A decrease in FEV1% is associated with a decrease in TLCO% and TLCO/VA.

In patients with mild and moderate COPD, there was no statistically significant correlation between FEV1% and diffusion capacity. Patients with very severe COPD, there was a statistically significant positive (direct) correlation between FEV1%, TLCO%, and TLCO/VA. A decrease in FEV1% is associated with a decrease in TLCO% and TLCO/VA (Table 5).

As regards the whole sample, there was a statistically significant positive (direct) correlation between

**Table 1 Mean, SD, and SE of different pulmonary function parameters of the whole sample**

| Bronchodilator | Pulmonary function | Mean±SD | SE |
|---|---|---|---|
| Pre | FVC% | 74.6±22.2 | 2.9 |
| | FEV1% | 47.9±20.2 | 2.6 |
| | $FEV_1$/FVC | 50.4±11.1 | 1.4 |
| | FEF25% | 27.2±23.1 | 3 |
| | FEF50% | 17.9±12.4 | 1.6 |
| | FEF75% | 17.3±7.6 | 1 |
| Post | FVC% | 80.2±22.5 | 2.9 |
| | FEV1% | 50.4±20.6 | 2.7 |
| | $FEV_1$/FVC | 49.4±11.4 | 1.5 |
| | FEF25% | 27.5±21.7 | 2.8 |
| | FEF50% | 19±14.1 | 1.8 |
| | FEF75% | 18.6±8.7 | 1.1 |

FEF, forced expiratory flow; $FEV_1$, forced expiratory volume in the first second; FVC, forced vital capacity.

**Table 2 Mean, SD, and SE of diffusion capacity of the whole sample**

| Diffusion capacity | Mean±SD | SE |
|---|---|---|
| TLCO | 59.2±22.6 | 2.9 |
| TLCO/VA | 1±0.4 | 0.05 |

COPD, chronic obstructive pulmonary disease; TLCO, transfer factor of the lung for carbon monoxide; TLCO/VA, transfer factor of the lung for carbon monoxide/alveolar volume ratio.

**Table 3 Statistical analysis using ANOVA test for comparison between diffusion capacity in patients with mild, moderate, and very severe COPD**

| Diffusion capacity | Mild COPD (*n*=7) (mean±SD) | Moderate COPD (*n*=24) (mean±SD) | Very severe COPD (*n*=29) (mean±SD) | *P*-value |
|---|---|---|---|---|
| TLCO% | 85.1±6.7$^a$ | 73±13.1$^a$ | 41.6±16.5$^b$ | <0.001* |
| TLCO/VA | 1.3±0.1$^a$ | 1.2±0.2$^a$ | 0.7±0.3$^b$ | <0.001* |

Different superscript letters indicate statistical difference between means. ANOVA, analysis of variance; COPD, chronic obstructive pulmonary disease; TLCO, transfer factor of the lung for carbon monoxide; TLCO/VA, transfer factor of the lung for carbon monoxide/alveolar volume ratio. *Significant at $P \leq 0.05$.

$FEV_1$/FVC, TLCO%, and TLCO/VA. A decrease in $FEV_1$/FVC is associated with a decrease in TLCO% and TLCO/VA.

In patients with mild, moderate, and very severe COPD, there was no statistically significant correlation between $FEV_1$/FVC and diffusion capacity (Table 6).

As regards the whole sample, there was a statistically significant positive (direct) correlation between FEF25%, TLCO%, and TLCO/VA. A decrease in FEF25% is associated with a decrease in TLCO% and TLCO/VA.

In patients with mild and moderate COPD, there was no statistically significant correlation between FEF25% and diffusion capacity. In patients with very severe COPD, there was a statistically significant positive (direct) correlation between FEF25%, TLCO%, and TLCO/VA. A decrease in FEF25% is associated with a decrease in TLCO% and TLCO/VA (Table 7).

As regards the whole sample, there was a statistically significant positive (direct) correlation between FEF50%, TLCO%, and TLCO/VA. A decrease in FEF50% is associated with a decrease in TLCO% and TLCO/VA.

In patients with mild and moderate COPD, there was no statistically significant correlation between FEF50%

**Table 4 Correlation between FVC% and diffusion capacity**

| Variables | Whole sample (*n*=60) | | Mild COPD (*n*=7) | | Moderate COPD (*n*=24) | | Very severe COPD (*n*=29) | |
|---|---|---|---|---|---|---|---|---|
| | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value |
| Diffusion capacity | | | | | | | | |
| TLCO% | 0.746 | <0.001* | –0.248 | 0.592 | –0.059 | 0.783 | 0.575 | 0.001* |
| TLCO/VA | 0.619 | <0.001* | 0.041 | 0.930 | –0.225 | 0.290 | 0.297 | 0.118 |

COPD, chronic obstructive pulmonary disease; FVC, forced vital capacity; TLCO, transfer factor of the lung for carbon monoxide; TLCO/VA, transfer factor/alveolar volume ratio. *Significant at $P\leq0.05$.

**Table 5 Correlation between FEV1% and diffusion capacity**

| Variables | Whole sample (*n*=60) | | Mild COPD (*n*=7) | | Moderate COPD (*n*=24) | | Very severe COPD (*n*=29) | |
|---|---|---|---|---|---|---|---|---|
| | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value |
| Diffusion capacity | | | | | | | | |
| TLCO | 0.775 | <0.001* | 0.571 | 0.180 | –0.082 | 0.704 | 0.526 | 0.003* |
| TLCO/VA | 0.750 | <0.001* | –0.036 | 0.939 | 0.090 | 0.674 | 0.419 | 0.024* |

COPD, chronic obstructive pulmonary disease; $FEV_1$, forced expiratory volume in the first second; TLCO, transfer factor of the lung for carbon monoxide; TLCO/VA, transfer factor of the lung for carbon monoxide/alveolar volume ratio. *Significant at $P\leq0.05$.

**Table 6 Correlation between $FEV_1$/FVC and diffusion capacity**

| Variables | Whole sample (*n*=60) | | Mild COPD (*n*=7) | | Moderate COPD (*n*=24) | | Very severe COPD (*n*=29) | |
|---|---|---|---|---|---|---|---|---|
| | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value |
| Diffusion capacity | | | | | | | | |
| TLCO | 0.456 | <0.001* | 0.500 | 0.253 | –0.070 | 0.747 | –0.087 | 0.655 |
| TLCO/VA | 0.559 | <0.001* | 0.010 | 0.998 | 0.218 | 0.305 | 0.115 | 0.554 |

COPD, chronic obstructive pulmonary disease; $FEV_1$, forced expiratory volume in the first second; FVC, forced vital capacity; TLCO, transfer factor of the lung for carbon monoxide; TLCO/VA, transfer factor of the lung for carbon monoxide/alveolar volume ratio. *Significant at $P\leq0.05$.

**Table 7 Correlation between FEF25% and diffusion capacity**

| Variables | Whole sample (*n*=60) | | Mild COPD (*n*=7) | | Moderate COPD (*n*=24) | | Very severe COPD (*n*=29) | |
|---|---|---|---|---|---|---|---|---|
| | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value |
| Diffusion capacity | | | | | | | | |
| TLCO% | 0.708 | <0.001* | 0.107 | 0.819 | –0.124 | 0.563 | 0.510 | 0.005* |
| TLCO/VA | 0.780 | <0.001* | 0.321 | 0.482 | 0.253 | 0.233 | 0.577 | 0.001* |

COPD, chronic obstructive pulmonary disease; FEF, forced expiratory flow; TLCO, transfer factor of the lung for carbon monoxide; TLCO/VA, transfer factor of the lung for carbon monoxide/alveolar volume ratio. *Significant at $P\leq0.05$.

and diffusion capacity. In patients with very severe COPD, there was a statistically significant positive (direct) correlation between FEF50%, TLCO%, and TLCO/VA. A decrease in FEF50% is associated with a decrease in TLCO% and TLCO/VA (Table 8).

In the whole sample, there was a statistically significant positive (direct) correlation between FEF75%, TLCO, and TLCO/VA. A decrease in FEF75% is associated with a decrease in TLCO and TLCO/VA.

In patients with mild, moderate, and very severe COPD, there was no statistically significant correlation between FEF75% and diffusion capacity (Table 9).

In the whole sample, there was a statistical significant negative (inverse) correlation between TLCO%, $PCO_2$, and $HCO_3$. A decrease in TLCO% is associated with an increase in $PCO_2$ and an increase in $HCO_3$. There was a statistically significant positive (direct) correlation between TLCO%, $PO_2$, and oxygen saturation (Sat $O_2$). A decrease in TLCO% is associated with a decrease in $PO_2$ and Sat $O_2$. There was no statistically significant correlation between TLCO% and pH.

In patients with mild COPD, there was no statistically significant correlation between TLCO and other variables. In patients with moderate COPD, there was no statistically significant correlation between TLCO% and other variables. In patients with very severe COPD, there was a statistically significant positive (direct) correlation between TLCO% and $PO_2$ and Sat $O_2$. There was no statistically significant correlation between TLCO% and other variables (Table 10).

As regards the whole sample, there was a statistically significant negative (inverse) correlation between TLCO/VA, $PCO_2$, and $HCO_3$. A decrease in TLCO/VA is associated with an increase in $PCO_2$ and an increase in $HCO_3$. There was a statistically significant positive (direct) correlation between TLCO/VA, $PO_2$, and Sat $O_2$. A decrease in TLCO/VA is associated with a decrease in $PO_2$ and Sat $O_2$. There was no statistically

**Table 8 Correlation between FEF50% and diffusion capacity**

| Variables | Whole sample (*n*=60) | | Mild COPD (*n*=7) | | Moderate COPD (*n*=24) | | Very severe COPD (*n*=29) | |
|---|---|---|---|---|---|---|---|---|
| | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value |
| Diffusion capacity | | | | | | | | |
| TLCO% | 0.709 | <0.001* | 0.464 | 0.294 | 0.067 | 0.757 | 0.412 | 0.026* |
| TLCO/VA | 0.745 | <0.001* | 0.107 | 0.819 | 0.297 | 0.1 59 | 0.403 | 0.030* |

COPD, chronic obstructive pulmonary disease; FEF, forced expiratory flow; TLCO, transfer factor of the lung for carbon monoxide; TLCO/VA, transfer factor of the lung for carbon monoxide/alveolar volume ratio. *Significant at $P \leq 0.05$.

**Table 9 Correlation between FEF75% and diffusion capacity**

| Variables | Whole sample (*n*=60) | | Mild COPD (*n*=7) | | Moderate COPD (*n*=24) | | Vert Severe COPD (*n*=29) | |
|---|---|---|---|---|---|---|---|---|
| | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value |
| Diffusion capacity | | | | | | | | |
| TLCO | 0.337 | 0.008* | 0.286 | 0.535 | 0.141 | 0.511 | 0.190 | 0.324 |
| TLCO/VA | 0.291 | 0.024* | 0.009 | 0.998 | 0.088 | 0.682 | 0.176 | 0.361 |

COPD, chronic obstructive pulmonary disease; FEF, forced expiratory flow; TLCO, transfer factor of the lung for carbon monoxide; TLCO/VA, transfer factor of the lung for carbon monoxide/alveolar volume ratio. *Significant at $P \leq 0.05$.

**Table 10 Correlation between (TLCO%) and blood gases**

| Variables | Whole sample (*n*=60) | | Mild COPD (*n*=7) | | Moderate COPD (*n*=24) | | Very Severe COPD (*n*=29) | |
|---|---|---|---|---|---|---|---|---|
| | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value |
| Blood gases | | | | | | | | |
| pH | 0.138 | 0.294 | -0.321 | 0.482 | 0.084 | 0.696 | –0.015 | 0.939 |
| $PCO_2$ | –0.353 | 0.006* | 0.143 | 0.688 | 0.081 | 0.706 | –0.346 | 0.066 |
| $PO_2$ | 0.349 | 0.006* | –0.464 | 0.294 | –0.010 | 0.965 | 0.380 | 0.042* |
| Sat $O_2$ | 0.361 | 0.005* | –0.378 | 0.403 | –0.053 | 0.805 | 0.400 | 0.031* |
| $HCO_3$ | –0.377 | 0.003* | 0.214 | 0.645 | –0.184 | 0.390 | –0.217 | 0.258 |

COPD, chronic obstructive pulmonary disease; $HCO_3$, bicarbonate; $PCO_2$, partial pressure of carbon dioxide; $PO_2$, partial pressure of oxygen; Sat $O_2$, oxygen saturation; TLCO, transfer factor of the lung for carbon monoxide. *Significant at $P \leq 0.05$.

**Table 11 Correlation between TLCO/VA and blood gases**

| Variables | Whole sample (*n*=60) | | Mild COPD (*n*=7) | | Moderate COPD (*n*=24) | | Very Severe COPD (*n*=29) | |
|---|---|---|---|---|---|---|---|---|
| | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value | Correlation coefficient (*r*) | *P*-value |
| Blood gases | | | | | | | | |
| pH | 0.105 | 0.424 | 0.286 | 0.535 | 0.147 | 0.493 | –0.107 | 0.582 |
| $PCO_2$ | –0.425 | 0.001* | 0.429 | 0.337 | –0.218 | 0.306 | –0.275 | 0.149 |
| $PO_2$ | 0.401 | 0.001* | –0.429 | 0.337 | 0.123 | 0.566 | 0.353 | 0.060 |
| Sat $O_2$ | 0.395 | 0.002* | –0.324 | 0.478 | 0.026 | 0.903 | 0.341 | 0.070 |
| $HCO_3$ | –0.392 | 0.002* | 0.357 | 0.432 | –0.200 | 0.350 | –0.174 | 0.367 |

COPD, chronic obstructive pulmonary disease; $HCO_3$, bicarbonate; $PCO_2$, partial pressure of carbon dioxide; $PO_2$, partial pressure of oxygen; Sat $O_2$, oxygen saturation; TLCO/VA, transfer factor of the lung for carbon monoxide/alveolar volume ratio. *Significant at $P \leq 0.05$.

significant correlation between TLCO/VA and pH (Table 11).

As regards patients with mild, moderate, and very severe COPD, there was no statistically significant correlation between TLCO/VA and other variables.

## Discussion

Spirometry is considered the gold standard for detecting and quantifying airflow obstruction in the general population. However, several studies have failed to find a strong association between the parenchymal destruction seen in emphysema and airflow obstruction as measured by $FEV_1$ [7]. This indicates that definitions that rely on measurement of $FEV_1$ alone may miss some cases of COPD. Including a measurement of DLco may be one way of detecting early cases of emphysema that otherwise would go undetected [8].

The DLco is a common and clinically useful test that provides a quantitative measure of gas transfer in the lungs. Diffusion capacity, along with spirometry and arterial blood gas measurement, is the core pulmonary function test used to evaluate and manage patients with respiratory diseases. Diffusion capacity is often abnormal in patients with interstitial lung disease, pulmonary vascular disease, and COPD [9].

The results show that TLCO% and TLCO/VA had no statistically significant difference between mild and moderate COPD groups, which showed the statistically significant highest mean values. The very severe COPD group showed the statistically significant lowest mean value. This agrees with the results of Polatlý *et al.* [10], who found that there was more rapid decline in TLCO in patients who also had excessive $FEV_1$ declines. DLco is an excellent test for differentiating COPD from asthma (DLco is low in moderate to severe COPD, whereas DLco is normal to high in asthma) [11].

There was a statistically significant positive (direct) correlation between FEV1%, TLCO%, and TLCO/VA in the whole sample. A decrease in FEV1% is associated with a decrease in TLCO% and TLCO/VA, which was similar to the study by Brashier *et al.* [12] to assess the correlation between FEV1% predicted and DLco% predicted in patients with varying severity of COPD. They found significant direct relation between FEV1% and DLco% predicted.

As regards patients with mild and moderate COPD, there were no statistically significant correlations between FEV1% and different variables. In patients with very severe COPD, there was a statistically significant positive (direct) correlation between FEV1%, TLCO%, and TLCO/VA. A decrease in FEV1% is associated with a decrease in TLCO% and TLCO/VA.Mohsenifar *et al.* [13] found that single measurements of TLCO in patients with COPD showed that a reduced value in early disease is associated with accelerated decline in $FEV_1$, and in advanced disease predicts exercise capacity and influences mortality.

As regards the whole sample, there was a statistically significant negative (inverse) correlation between TLCO%, $PCO_2$, and $HCO_{3za}$. A decrease in TLCO% is associated with an increase in $PCO_2$ and an increase in $HCO_3$.

There was a statistically significant positive (direct) correlation between TLCO%, $PO_2$, and Sat $O_2$. A decrease in TLCO% is associated with a decrease in $PO_2$ and Sat $O_2$. This agreed with the results of Mohsenifar *et al.* [13] to assess single-breath diffusion capacity of the lung for carbon monoxide as a predictor of $PaO_2$ at maximum work rate, and walking distance in patients with COPD, wherein a highly statistically significant direct relation between DLco and $PaO_2$ was found. This agrees with the results of Knower *et al.* [14], who found that DLco of less than 50% predicted is highly suggestive of exercise desaturation, with a sensitivity of 89%. Desaturation was more closely associated with reduced DLco than with reduced resting Sat $O_2$.

## Conclusion

Reduced DLco plus airflow obstruction together identifies a group of individuals with significantly worse lung function. The combination of lung function measurements reflecting bronchial collapsibility, lung diffusion capacity, and bronchodilator response tests is useful for assessing and monitoring parenchymal damage in COPD patients and is a good estimate of the extent of emphysema.

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### Conflicts of interest

There are no conflicts of interest.

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