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# THE EPP LIGHT STUDY: A SURVEY DESCRIBING THE BURDEN OF ERYTHROPOIETIC PROTOPORPHYRIA

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## INTRODUCTION

- Erythropoietic protoporphyria and X-linked protoporphyria (collectively referred to as EPP) are rare, genetic disorders of the heme biosynthetic pathway, leading to toxic accumulation of the metabolite protoporphyrin IX (PPIX).
- Clinically, EPP presents with painful phototoxic reactions upon light exposure. In some patients, PPIX accumulation in the liver can lead to hepatobiliary disease, which can progress to liver failure, and lead to liver and/or bone marrow transplantation.
- To date, little has been published on the burden of EPP from the patient perspective.

## AIMS

The EPP LIGHT Study sought to comprehensively describe the burden in all facets of life, including symptoms, health-related quality-of life (HRQoL) (e.g., emotional functioning, satisfaction, social isolation), work loss, and healthcare resource utilization (HCU) in adults and adolescents with EPP.

## METHODS

- Participants, recruited by the United Porphyrins Association (UPA), were ≥12 years of age, reported a diagnosis of EPP, resided in North America, were able to speak, read, and write English, and were able to complete a one-time online questionnaire.
- Data collection took place in May – July 2024.
- Online questionnaire included existing, validated, and original patient-reported outcome measures developed based on qualitative research with individuals with EPP (Mathias et al., 2024).
- WCG IRB approved the study; informed consent was obtained from all participants.

## RESULTS

### Background Characteristics (See Table 1)

- Most adults took longer to be diagnosed with EPP than adolescents
- Both adults and adolescents had seen multiple doctors prior to their diagnosis
- A considerable number of adults had liver disease and gallstones
- Some adults and adolescents rated their health “much worse” than those without EPP

**Table 1: Background Characteristics**

Characteristic	Adults (n=164)	Adolescents (n=33)
Gender (% female)	60%	49%
Race (% white)	96%	100%
Ethnicity (% non-Hispanic/Latino)	92%	88%
Education (%)		
- College degree or higher	64%	0%
- Some college	20%	0%
- High school or equivalent	16%	25%
- Middle school or equivalent	1%	75%
Marital Status (% married)	56%	N/A
Work full-time (%)	54%	6%
Attend school full-time (%)	7%	91%
Mean age at diagnosis (years)	15	6
Time to diagnosis (years)	63% (≥5 years)	70% (≤4 years)
Mean number of physicians seen prior to diagnosis (mean ± SD)	3.2 ± 1.9	2.6 ± 1.6
Common co-morbid conditions (%)		
- Vitamin D deficiency	59%	42%
- Anemia	58%	30%
- Gallstones	31%	0%
- Liver disease (defined as elevated liver enzymes, liver fibrosis)	15%	3%
- No co-morbid conditions	13%	36%

Abbreviations: N/A: Not applicable; SD: standard deviation

### Prodromal Symptoms

- 49% of adults and 15% of adolescents experience prodromal symptoms after spending ≤10 minutes in direct or indirect sunlight
- 73% of adults and 82% of adolescents experienced ≥1 prodromal symptoms in the past 3 months
- 48% of the full sample (37% of adults and 79% of adolescents) reported that prodromal symptoms affect their ability to do daily activities at least “quite a bit”
- The most common prodromal symptoms experienced by adults were tingling (70%), feelings of warmth (57%), itching (55%), stinging (53%) and sensitivity to touch (53%). Most prodromal symptoms experienced by adults were rated “moderate” (≥ 35%) or “severe” (≥15%)
- The most common prodromal symptoms experienced by adolescents were tingling (76%), sensitivity to hot/cold (67%), burning (61%), and itching, sensitivity to touch, and pain (all 58%). Most prodromal symptoms experienced by adolescents were rated as “moderate” (≥25%) or “severe” (≥25%)

### Phototoxic Reactions

- Most adults (67%) and adolescents (88%) experienced ≥1 phototoxic reaction in the past 12 months
- 68% of adults and 45% of adolescents experienced pain from a phototoxic reaction after <30 minutes in direct sunlight
- 58% of adults and 30% of adolescents reported their last phototoxic reaction affected their ability to do daily activities “very much”
- After a phototoxic reaction, it took on average 5.5 ± 4.8 days (adults) and 5.1 ± 3.0 days (adolescents) for all symptoms to improve

### Satisfaction with Social Roles and Activities & Social Isolation

The T-scores for adults on the PROMIS Satisfaction with Social Roles and Activities SF-8a and PROMIS Social Isolation-4a were 43.4 ± 9.3 and 55.5 ± 9.4, respectively. T-scores for adolescents on the PROMIS Satisfaction with Social Roles and Activities was 46.9 ± 7.5. Mean values for adults and adolescents was substantially worse (lower) for Satisfaction with Social Roles and Activities and worse (higher) for adults for Social Isolation than the general population score of 50 ± 10. A difference of >3 points is considered meaningful (Terwee et al., 2021). On the PROMIS Satisfaction with Social Roles and Activities, 72% of adults and 45% of adolescents scored lower (worse) than a 47 (the threshold for what is considered meaningful). On the PROMIS Social Isolation, 63% of adults scored higher (worse) than 53 (the threshold for what is considered meaningful).

### Emotional Functioning

- The majority of adults and adolescents reported feeling depressed or sad (75% adults, 46% adolescents), anxious (80%, 61%), isolated (83%, 58%), frustrated (90%, 94%), and lonely (76%, 39%)

### Work/School

- Adults and adolescents reported meaningful amounts of time lost from work/school (see Table 2)

**Table 2: Work and School Loss**

	Adults (n=164)	Adolescents (n=33)
Currently employed, yes (%)	66% (n=108)	18% (n=6)
Hours of work missed in past month due to EPP (mean ± SD)	4.6 ± 13.6	0 ± 0
Missed work due to EPP	23% (n=108)	0% (n=0)
Currently attending school, yes (%)	13% (n=21)	73% (n=24)
Hours of school missed due in EPP in past month (mean ± SD)	3.3 ± 6.5	5.0 ± 9.3
Missed school due to EPP, yes (%)	24% (n=5)	42% (n=10)

### Physician Visits Due to Issues Related to EPP

Both adults and adolescents reported a moderate number of visits to physicians in the past 12 months, although adults tended to have more visits (Table 3).

**Table 3: Physician Visits due to EPP in the last 12 months**

Number of Visits in past 12 month (Mean ± SD)	Adults (N=164)	Adolescents (N=33)
Total physician visits	8.0 ± 13.3 (n=134)	3.2 ± 2.9 (n=25)
Hematologist	3.3 ± 5.3 (n=52)	2.8 ± 3.5 (n=4)
General practitioner/Internist	3.2 ± 4.8 (n=76)	2.0 ± 0.9 (n=8)
Dermatologist	2.8 ± 2.2 (n=60)	1.5 ± 0.9 (n=15)
Hepatologist	4.6 ± 13.0 (n=29)	1.0 ± 0 (n=2)

### Hospitalizations/ER Visits in Past 12 Months Due to EPP

- 14 adults (8.6%) reported an ER visit, and 10 adults (6.1%) reported a hospitalization in the past 12 months due to EPP. Adolescents did not report any ER visits or hospitalizations in the past 12 months
- Mean number of ER visits and hospitalizations for adults was 5.4 ± 10.2 and 2.2 ± 1.5, respectively
  - Reason(s) for ER visit was pain from a reaction (71%) and/or problems with liver (50%)
  - Reason(s) for hospitalization was pain from a phototoxic reaction (70%) and/or problems with liver (70%).

## LIMITATIONS

Diagnosis of EPP self-reported (not confirmed by physician); participants recruited by UPA, with presumably more engaged individuals than an average individual with EPP; only individuals from North America were enrolled. Different results may have been obtained from a more diverse population.

## CONCLUSIONS

Adults and adolescents with EPP experience multiple symptoms that impact all facets of their lives, including the ability to be out in the sunlight for prolonged periods of time, ability to undertake daily activities, deficits in emotional functioning, and absenteeism at work and school. These lead to excess HCU and significant burden to individuals with EPP.

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## REFERENCES

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## CONTACT INFORMATION

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