

Chemotherapy-Induced Hand–Foot Syndrome: A Narrative Review of Prevention, Assessment, and Evidence-Based Nursing Management

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ABSTRACT

Background: Chemotherapy-induced Hand–Foot Syndrome (HFS), also known as palmar-plantar erythrodysesthesia, is a common dose-limiting cutaneous toxicity associated with several anticancer agents, particularly capecitabine, 5-fluorouracil, pegylated liposomal doxorubicin, and multikinase inhibitors. HFS can significantly impair patients' physical function, activities of daily living, treatment adherence, and overall quality of life. Early recognition, appropriate assessment, preventive interventions, and evidence-based nursing management are essential to minimize symptom severity and optimize treatment outcomes.¹²

Methods: A narrative review methodology was adopted to synthesize current evidence regarding chemotherapy-induced HFS. Electronic databases, including PubMed, Scopus, Web of Science, and Google Scholar, were searched for English-language articles published between 2000 and 2025. Original research articles, clinical guidelines, systematic reviews, meta-analyses, and evidence-based practice recommendations focusing on prevention, assessment, and management of HFS were included. The evidence was synthesized narratively according to major thematic areas.

Results: The reviewed literature demonstrates that HFS is a multifactorial adverse effect resulting from the accumulation of chemotherapeutic agents in the skin, leading to inflammation and damage to keratinocytes and eccrine sweat glands. Early identification through standardized grading systems, patient education, prophylactic skin care, dose modification, topical therapies, and multidisciplinary nursing interventions effectively reduce symptom severity and improve treatment adherence. Evidence also supports the role of structured nursing assessment, patient counseling, and individualized supportive care in improving quality of life.

Conclusion: Chemotherapy-induced HFS remains a clinically significant toxicity affecting cancer treatment and patient well-being. Comprehensive prevention strategies, standardized assessment tools, and evidence-based nursing management are essential for minimizing treatment interruptions and improving clinical outcomes. Further high-quality prospective studies are needed to strengthen current recommendations and optimize supportive care practices.

Keywords: Hand–Foot Syndrome; Palmar-Plantar Erythrodysesthesia; Chemotherapy; Nursing Management; Prevention; Oncology Nursing.

INTRODUCTION

Cancer remains one of the leading causes of morbidity and mortality worldwide, and advances in systemic anticancer therapy have substantially improved survival outcomes across many malignancies. Despite these therapeutic advances, chemotherapy-related adverse effects continue to represent a major challenge affecting treatment adherence, quality of life, and overall clinical outcomes. Among these toxicities, chemotherapy-induced Hand–Foot Syndrome (HFS), also known as palmar-plantar erythrodysesthesia (PPE), is one of the most common dermatologic complications associated with several cytotoxic and targeted anticancer agents.¹

Hand–Foot Syndrome is characterized by painful erythema, swelling, numbness, tingling, dysesthesia, blistering, desquamation, and hyperkeratosis affecting the palms of the hands and soles of the feet. Symptoms usually develop after repeated chemotherapy exposure and may progressively worsen if early preventive measures are not implemented. Severe HFS frequently interferes with walking, manual activities, self-care, occupational functioning, and activities of daily living, resulting in significant physical and psychological distress.²

The incidence of HFS varies according to the chemotherapeutic agent, cumulative dose, treatment schedule, and patient-related factors. Capecitabine, continuous-infusion 5-fluorouracil, pegylated liposomal doxorubicin, cytarabine, docetaxel, and several multikinase inhibitors such as sorafenib and sunitinib are among the drugs most commonly associated with this toxicity. Reported incidence ranges from approximately 20% to 60%, with severe (Grade 3) reactions occurring in a smaller but clinically significant proportion of patients.³

Although the precise pathophysiological mechanisms remain incompletely understood, current evidence suggests that local accumulation of chemotherapeutic agents within eccrine sweat glands, repeated mechanical stress, vascular injury, inflammatory cytokine release, and direct toxicity to rapidly proliferating epidermal cells contribute to the development of HFS. Individual susceptibility may also be influenced by age, nutritional status, genetic polymorphisms, pre-existing peripheral neuropathy, and treatment-related factors.²

Standardized assessment plays an essential role in the early recognition and management of HFS. Clinical grading systems, including the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE Version 5.0) and patient-reported outcome measures such as the Hand–Foot Syndrome-14 (HFS-14) questionnaire, facilitate accurate evaluation of symptom severity, functional impairment, and treatment response. Early identification allows timely implementation of supportive care interventions before severe toxicity develops.⁴

Evidence-based management of HFS includes preventive skin care, patient education, avoidance of mechanical friction and heat exposure, routine use of emollients, topical corticosteroids for inflammatory symptoms, pain management, and chemotherapy dose modification when clinically indicated. Oncology nurses play a central role in patient education, early symptom recognition, toxicity assessment, implementation of supportive care interventions, monitoring treatment response, and promoting adherence to prescribed anticancer therapy. Their contribution is fundamental to minimizing treatment interruptions and improving patient-centered outcomes.¹²

Given the increasing use of oral fluoropyrimidines and targeted anticancer therapies, HFS has become an increasingly important supportive care issue in oncology practice. A comprehensive synthesis of current evidence is therefore necessary to guide healthcare professionals in implementing effective prevention strategies and evidence-based nursing management.

The objective of this narrative review is to summarize the current evidence regarding chemotherapy-induced Hand–Foot Syndrome, with particular emphasis on its epidemiology, pathophysiology, risk factors, clinical manifestations, assessment, prevention, and evidence-based nursing management to support optimal patient care and improve treatment outcomes.

METHODOLOGY

Study Design

A narrative review methodology was adopted to identify, critically appraise, and synthesize current evidence regarding chemotherapy-induced Hand–Foot Syndrome, with particular emphasis on prevention, assessment, and evidence-based nursing management.

Search Strategy

A comprehensive literature search was conducted using electronic databases including PubMed, Scopus, Web of Science, CINAHL, Google Scholar, and Cochrane Library. Articles published in English between January 2000 and June 2025 were searched. The search strategy included combinations of Medical Subject Headings (MeSH) and free-text keywords using Boolean operators (AND/OR), including:

Hand–Foot Syndrome

- "Palmar-Plantar Erythrodysesthesia"
- "Chemotherapy-Induced Hand–Foot Syndrome"
- Capecitabine"
- "5-Fluorouracil"
- "Cancer Nursing"
- "Oncology Nursing"
- "Evidence-Based Nursing"
- "Supportive Care"
- "Prevention"
- "Assessment"
- "Management"

Manual searching of reference lists from eligible articles and international oncology guidelines was also performed to identify additional relevant publications.

Eligibility Criteria

Inclusion Criteria

- Original research studies
- Randomized controlled trials
- Prospective and retrospective observational studies
- Cohort and cross-sectional studies
- Systematic reviews and meta-analyses
- International clinical practice guidelines
- English-language publications focusing on chemotherapy-induced Hand–Foot Syndrome

Exclusion Criteria

- Conference abstracts without full text
- Editorials
- Letters to the editor
- Case reports

- Animal studies
- Non-English publications
- Studies unrelated to chemotherapy-induced Hand–Foot Syndrome

Study Selection

Titles and abstracts retrieved through database searches were screened independently for relevance. Full-text articles meeting the inclusion criteria were subsequently reviewed in detail. Relevant studies addressing epidemiology, pathophysiology, risk factors, clinical manifestations, assessment, prevention, pharmacological management, non-pharmacological interventions, and nursing management were included in the narrative synthesis.

Data Extraction

Data extracted from eligible studies included author, year of publication, study design, country, sample characteristics, chemotherapeutic agent investigated, assessment tools, interventions, primary outcomes, and key findings relevant to Hand–Foot Syndrome prevention and management.

Data Synthesis

The findings were synthesized narratively and organized into the following thematic domains:

- Epidemiology
- Pathophysiology
- Risk Factors
- Clinical Manifestations
- Assessment and Grading Systems
- Prevention Strategies
- Pharmacological Management
- Non-pharmacological Management
- Evidence-Based Nursing Management
- Future Research Directions

RESULTS**Overview of Included Evidence**

The literature reviewed indicates that chemotherapy-induced Hand–Foot Syndrome (HFS) is a common dermatologic toxicity associated with fluoropyrimidines, anthracyclines, and several targeted anticancer agents. The incidence, severity, and clinical presentation vary according to the chemotherapeutic agent, dosage, treatment duration, and individual patient characteristics. Across the reviewed studies, evidence consistently demonstrated that early identification, patient education, preventive skin care, timely dose modification, and multidisciplinary supportive care significantly reduce HFS severity and improve treatment adherence.^{5–7}

For ease of presentation, the findings were synthesized under the following themes:

Epidemiology, Pathophysiology, Risk Factors, Clinical Manifestations Assessment and Grading, Prevention, Pharmacological Management, Non-pharmacological Management, Evidence-Based Nursing Management

Epidemiology

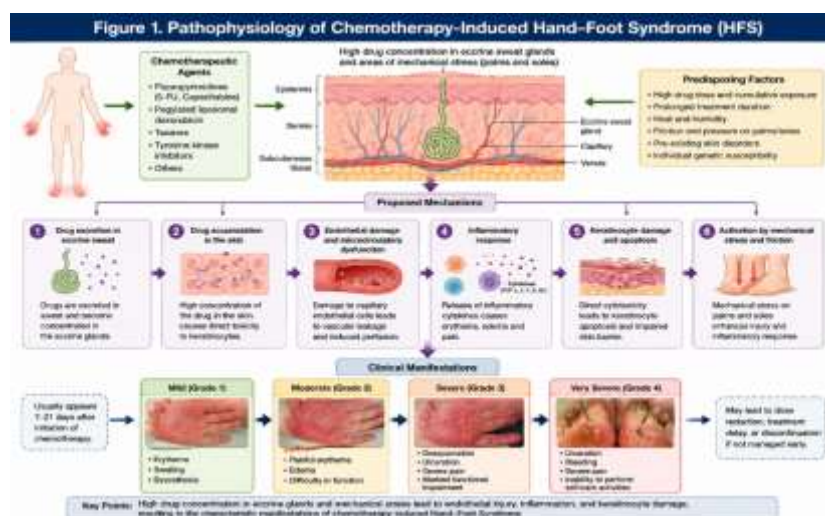
Hand–Foot Syndrome is among the most frequent dose-limiting adverse effects of several systemic anticancer therapies. The reported incidence ranges from **20% to 60%** among patients receiving capecitabine and continuous-infusion 5-fluorouracil, whereas pegylated liposomal doxorubicin has been

associated with incidences exceeding 50% in some treatment protocols. Multikinase inhibitors such as sorafenib, sunitinib, regorafenib, and cabozantinib also produce characteristic palmoplantar skin toxicity, although the clinical features may differ slightly from classical chemotherapy-induced HFS.⁵⁻⁸

The occurrence of HFS is influenced by cumulative drug exposure, dosing schedule, treatment duration, and combination chemotherapy. Elderly patients, individuals with poor performance status, and those receiving prolonged oral chemotherapy are at increased risk of developing moderate-to-severe HFS.⁸

Pathophysiology

Although the exact mechanism remains incompletely understood, HFS is believed to result from multiple interacting biological processes. Following systemic administration, chemotherapeutic agents accumulate preferentially within the eccrine sweat glands of the palms and soles. Because these regions contain abundant eccrine glands and are subjected to constant pressure and friction, higher local drug concentrations develop, leading to direct injury of basal keratinocytes and vascular endothelial cells.⁹ Mechanical stress during walking and manual activities further increases local tissue damage, promoting inflammatory cytokine release, oxidative stress, apoptosis of epidermal cells, and impairment of skin barrier integrity. Histopathological findings commonly include epidermal necrosis, vacuolar degeneration of basal keratinocytes, dermal edema, vascular dilation, and inflammatory cell infiltration.¹⁰ Current evidence also suggests that genetic polymorphisms affecting fluoropyrimidine metabolism, particularly dihydropyrimidine dehydrogenase (DPD) deficiency, may increase susceptibility to severe HFS.¹¹



Risk Factors

Multiple patient-related and treatment-related factors contribute to the development of HFS.

Patient-related factors

- Advanced age
- Female sex
- Poor nutritional status
- Diabetes mellitus
- Peripheral vascular disease
- Pre-existing peripheral neuropathy
- Reduced renal function
- Genetic variations affecting fluoropyrimidine metabolism¹¹⁻¹³

Treatment-related factors

- High cumulative chemotherapy dose
- Continuous drug administration
- Oral capecitabine therapy
- Continuous infusion 5-fluorouracil
- Pegylated liposomal doxorubicin
- Combination chemotherapy
- Long treatment duration
- Concurrent targeted therapy¹²

Recognition of these risk factors allows clinicians to identify high-risk patients and implement individualized preventive interventions before symptom onset.

Clinical Manifestations

Clinical symptoms usually appear within the first two to six weeks after initiation of chemotherapy but may occur earlier during subsequent treatment cycles.

Early manifestations include:

- Tingling sensation
- Numbness
- Burning pain
- Dysesthesia
- Increased sensitivity
- Mild erythema

As toxicity progresses, patients develop:

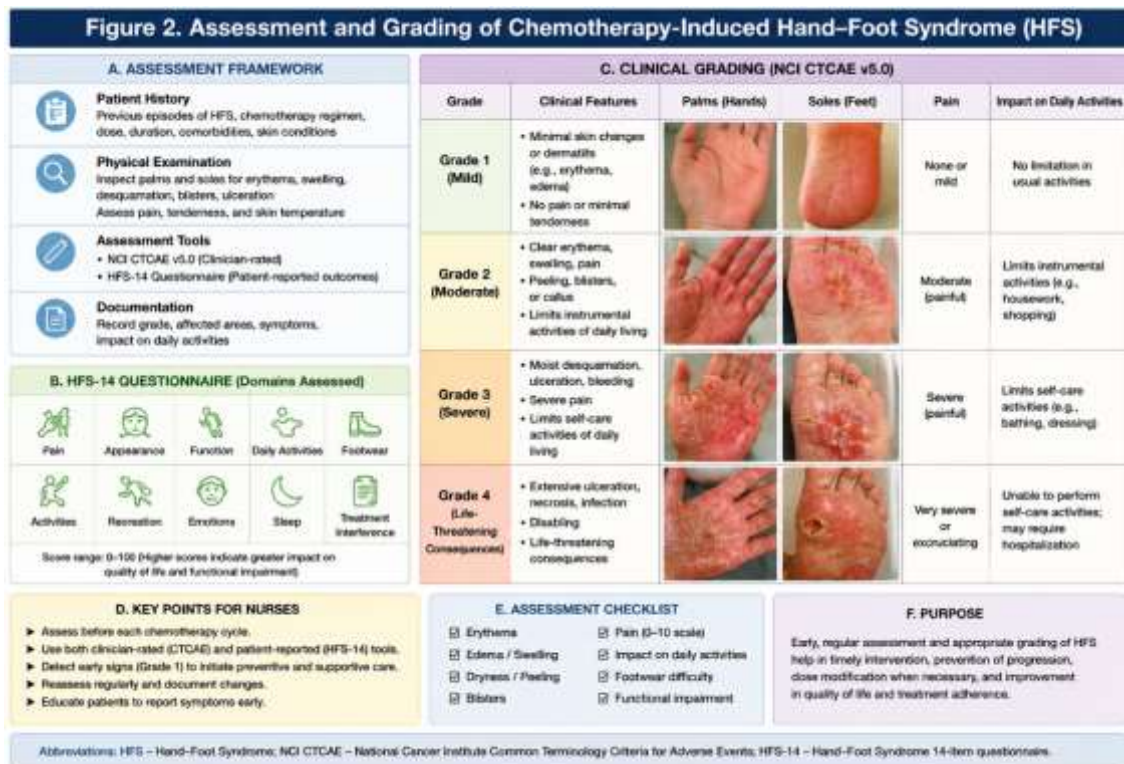
- Symmetrical redness
- Swelling
- Severe pain
- Blister formation
- Dryness
- Hyperkeratosis
- Skin fissures
- Desquamation
- Difficulty walking
- Impaired hand function

Grade 3 HFS is characterized by severe pain and extensive skin changes that interfere with activities of daily living and frequently require chemotherapy interruption or dose reduction.⁶¹⁰

Assessment and Grading

Early assessment is essential to prevent progression to severe toxicity.

The **National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE Version 5.0)** remains the most widely used clinician-reported grading s



The **Hand-Foot Syndrome-14 (HFS-14)** questionnaire evaluates:

- Pain
- Functional disability
- Walking ability
- Hand function
- Emotional well-being
- Social participation
- Daily activities
- HFS-14 has demonstrated excellent reliability and validity for measuring quality-of-life impairment associated with chemotherapy-induced HFS and is increasingly recommended for routine clinical assessment.¹⁵

Prevention Strategies

Current evidence supports several preventive interventions.

These include:

- Routine use of fragrance-free emollients
- Daily skin moisturization
- Avoidance of excessive heat exposure
- Avoidance of prolonged walking
- Wearing comfortable footwear
- Avoiding tight-fitting gloves
- Early reporting of symptoms
- Regular skin inspection
- Dose adjustment in high-risk patients
- Patient education before initiation of chemotherapy⁶¹⁶

Several randomized clinical trials have evaluated topical urea-containing creams, showing reductions in HFS incidence and delayed onset among patients receiving capecitabine therapy.¹⁷

Pharmacological Management

Management depends on severity.

Evidence supports the use of:

- Urea-based moisturizers
- Topical corticosteroids
- Topical keratolytic agents
- Topical analgesics
- Oral analgesics
- Pyridoxine (limited evidence)
- Celecoxib in selected patients
- Chemotherapy dose interruption or reduction for Grade 2–3 toxicity⁶¹⁸

Although pyridoxine has historically been prescribed, current systematic reviews report inconsistent benefit, and routine use is not universally recommended.

Non-Pharmacological Management

Supportive care measures remain essential throughout treatment.

Recommended interventions include:

- Cooling hands and feet during chemotherapy infusion
- Avoiding repetitive friction
- Limiting vigorous exercise
- Daily skin assessment
- Adequate hydration
- Gentle cleansing
- Protective footwear
- Cotton gloves for household work
- Prompt treatment of skin fissures
- Psychological support¹⁶

These interventions reduce mechanical trauma and improve patient comfort without interfering with anticancer treatment.

Evidence-Based Nursing Management

Oncology nurses play a central role in preventing and managing chemotherapy-induced HFS.

Key nursing responsibilities include:

- Baseline skin assessment before chemotherapy, Identification of high-risk patients, Patient education regarding early symptoms, Teaching preventive skin care measures, Monitoring symptom progression during every treatment cycle, Assessment using NCI-CTCAE and HFS-14, Documentation of toxicity grades, Reinforcement of adherence to supportive care, Coordination with oncologists regarding dose modification, Emotional support and counselling, Education regarding activities of daily living. Studies consistently demonstrate that nurse-led education programs improve early symptom recognition, reduce severe HFS, enhance treatment adherence, and improve health-related quality of life. Comprehensive nursing care therefore represents a cornerstone of evidence-based supportive oncology practice.^{615–18}

DISCUSSION

Chemotherapy-induced Hand–Foot Syndrome (HFS) is a clinically significant dermatologic toxicity that adversely affects patients undergoing systemic anticancer therapy. Although HFS is not usually life-threatening, it substantially impairs functional ability, quality of life, and adherence to chemotherapy. The evidence synthesized in this review demonstrates that the development of HFS is influenced by multiple factors, including the type of chemotherapeutic agent, cumulative drug exposure, treatment duration, patient-related characteristics, and individual susceptibility.¹⁹

Fluoropyrimidines, particularly capecitabine and continuous-infusion 5-fluorouracil, remain the agents most frequently associated with HFS. Pegylated liposomal doxorubicin and several multikinase inhibitors have also been consistently linked to this adverse effect. Although the exact pathophysiological mechanisms remain incompletely understood, available evidence supports the involvement of eccrine sweat gland drug accumulation, repeated mechanical stress, endothelial injury, inflammatory cytokine release, and epidermal cell damage. These mechanisms explain the preferential involvement of the palms and soles, which are exposed to constant pressure and friction during daily activities.^{9,19}

Clinical manifestations range from mild erythema and dysesthesia to painful ulceration and severe functional impairment. If left untreated, HFS may necessitate chemotherapy dose reduction, treatment delay, or complete discontinuation, potentially compromising cancer treatment outcomes. Therefore, prompt recognition and early intervention are essential to prevent progression to severe toxicity.¹⁴

Standardized assessment tools facilitate accurate evaluation of HFS severity and guide clinical decision-making. The National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE Version 5.0) remains the most widely accepted clinician-reported grading system for toxicity assessment. However, clinician-based grading alone may underestimate the patient's symptom burden. Patient-reported outcome measures such as the Hand–Foot Syndrome-14 (HFS-14) questionnaire complement clinical assessment by evaluating pain, functional disability, emotional well-being, and quality of life. The combined use of clinician-reported and patient-reported assessments provides a more comprehensive evaluation of treatment-related toxicity.¹⁵ Preventive strategies represent the cornerstone of HFS management. Evidence supports routine skin moisturization with urea-containing emollients, avoidance of excessive friction and heat exposure, early patient education, and regular skin assessment. Several studies have demonstrated that these interventions delay symptom onset and reduce HFS severity. Chemotherapy dose modification remains the most effective intervention for moderate-to-severe HFS and should be implemented promptly when clinically indicated to prevent irreversible skin damage while maintaining therapeutic efficacy.¹⁷

The role of oncology nurses extends beyond symptom assessment to include patient education, counseling, preventive care, treatment monitoring, psychosocial support, and multidisciplinary communication. Nurse-led interventions improve early symptom recognition, promote adherence to supportive care recommendations, reduce treatment interruptions, and enhance patients' quality of life. Education regarding appropriate skin care, activity modification, footwear selection, and timely reporting of symptoms empowers patients to participate actively in self-management and contributes to better clinical outcomes.²¹

Despite growing evidence supporting preventive and supportive interventions, important knowledge gaps remain. Considerable heterogeneity exists among published studies with respect to HFS grading systems, intervention protocols, outcome measures, and study populations. Furthermore, evidence regarding pharmacological interventions such as pyridoxine remains inconsistent, highlighting the need for

additional high-quality randomized controlled trials. Future research should focus on standardized assessment methods, personalized prevention strategies, pharmacogenomic predictors of toxicity, and innovative supportive care interventions that optimize patient-centered outcomes.

LIMITATIONS

This narrative review has several limitations. Only English-language publications were included, which may have excluded relevant evidence published in other languages. The included studies varied considerably in design, patient populations, chemotherapy regimens, and outcome measures, limiting direct comparison across studies. Because this review adopted a narrative rather than systematic methodology, formal risk-of-bias assessment and quantitative meta-analysis were not performed. Finally, emerging evidence published after the search period may not have been captured.

FUTURE RECOMMENDATIONS

Future research should focus on:

- Conducting large multicenter randomized controlled trials evaluating preventive interventions for chemotherapy-induced HFS.
- Standardizing HFS assessment using validated clinician-reported and patient-reported outcome measures.
- Investigating pharmacogenomic markers associated with susceptibility to severe HFS.
- Evaluating long-term quality-of-life outcomes among cancer survivors experiencing HFS.
- Developing evidence-based nursing protocols for early detection and management of HFS.
- Assessing the effectiveness of telehealth-based symptom monitoring and digital patient education programs.
- Investigating novel topical and systemic therapies for prevention and treatment of chemotherapy-induced HFS.

CONCLUSION

Chemotherapy-induced Hand–Foot Syndrome remains one of the most common dose-limiting toxicities associated with fluoropyrimidines, pegylated liposomal doxorubicin, and several targeted anticancer therapies. Although HFS rarely threatens survival, its impact on physical functioning, treatment adherence, and health-related quality of life is substantial. Current evidence demonstrates that early identification, standardized assessment, patient education, preventive skin care, and timely chemotherapy dose modification effectively reduce symptom severity and minimize treatment interruptions. Oncology nurses play a pivotal role in the comprehensive management of HFS through systematic assessment, implementation of preventive strategies, patient counseling, symptom monitoring, psychosocial support, and multidisciplinary collaboration. The integration of evidence-based nursing interventions into routine oncology practice contributes significantly to improved patient outcomes and quality of life. Further high-quality clinical research is required to establish standardized prevention protocols, evaluate emerging therapeutic interventions, and strengthen evidence-based supportive care recommendations. A patient-centered, multidisciplinary approach remains essential for optimizing the prevention and management of chemotherapy-induced Hand–Foot Syndrome.

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