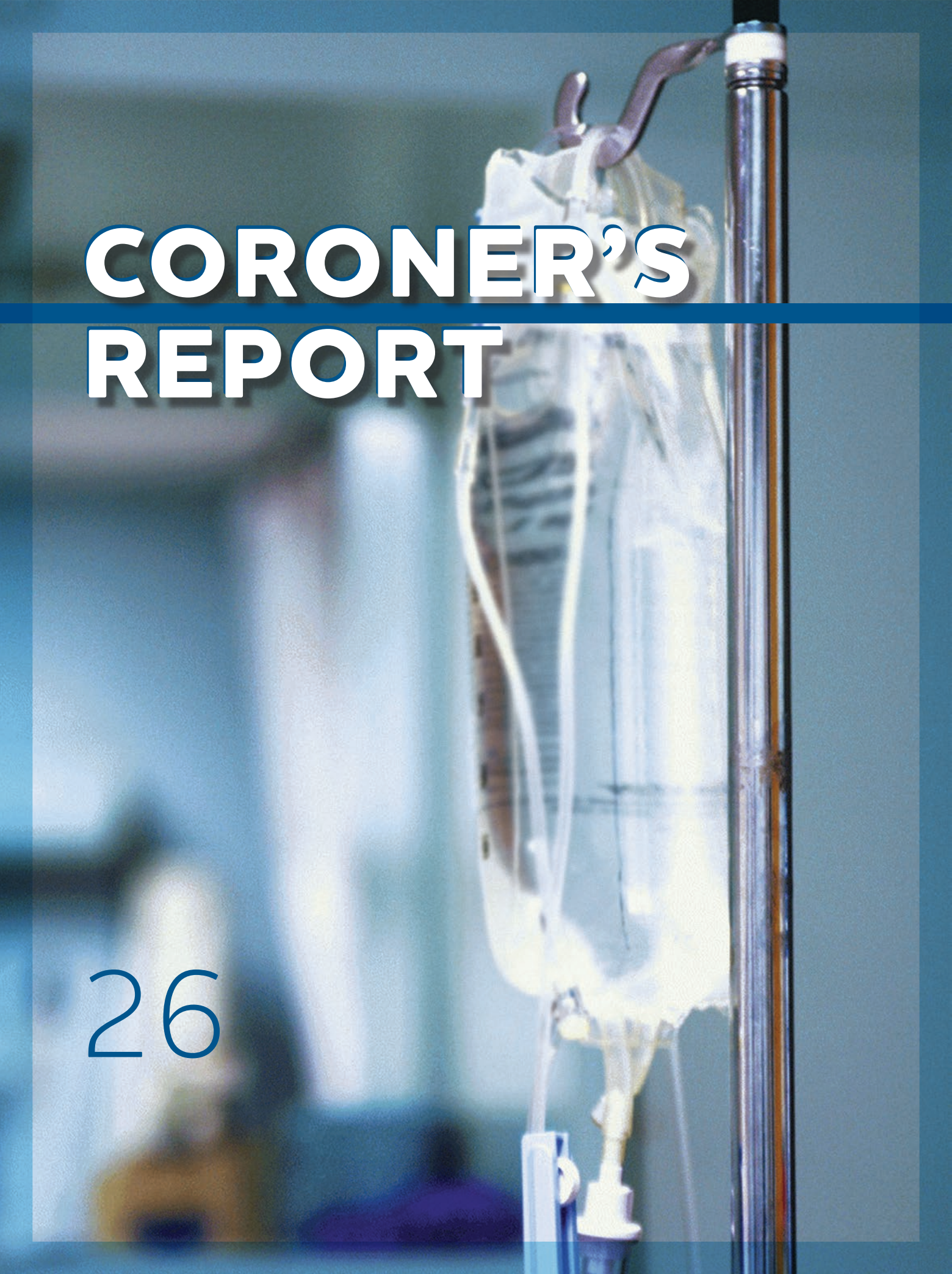

CORONER'S REPORT

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THE CORONER HAS RECOMMENDED THAT THE ONTARIO COLLEGE OF PHARMACISTS EDUCATE CLINICIANS ON THE DEFINITION OF OPIOID TOLERANCE, AND REVIEW THE PATIENT CONDITIONS AND COMORBIDITIES THAT MAY SUGGEST THE NEED FOR REDUCED DOSE OF OPIOIDS.

CASE SUMMARY

A 100-year old woman, with no recognized chronic medical issues, died four days after being admitted to hospital for weakness and pain in her buttock radiating to her abdomen. The reported cause of death was acute overdose of HYDROmorphone as a result of a medication error complicating the treatment of hepatocellular carcinoma in association with micronodular cirrhosis.

Case history: Prior to admission to hospital, the patient was living in a retirement residence in good health. She used a walker for mobility and her only prescribed medication was oxazepam 15 mg orally at bedtime as needed for nighttime sedation. A consultant note indicated she had also been taking acetaminophen for buttock pain that she attributed to a muscle strain after an exercise class. The patient was transferred to a local emergency department with weakness and pain in her buttock, radiating to her abdomen. On exam she was found to have a hemoglobin of 64, melena, and liver dysfunction. A liver mass was noted on CT and MRI.

Course in Hospital: On the day of admission, the patient's abdominal discomfort escalated and that evening she was ordered an antacid and a local anesthetic.

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Later that evening, she became agitated and was moved to the nursing station for monitoring.

The following morning, the patient was ordered haloperidol 0.5 mg hs (no route specified, oral assumed) for agitation, morphine 1 mg IV q1h prn pain with instructions to increase to 3mg q1h prn pain, dimenhydrinate 25 mg IV prn nausea. A physician note indicated that the situation was quite grave, the CT suggested significant intra-abdominal pathology and there were plans for an MRI and follow-up with a family member.

Based on her clinical situation, a decision was made to transition the patient to palliative care. The patient was started on oral morphine for pain control. On the second day in hospital, the patient received morphine (1 mg x 1 dose) at 1:15 p.m. The next day, the patient received 1mg morphine at 9 a.m., 2mg of morphine at 12:55p.m., and 3mg morphine at 6:10p.m.

At 6:00 a.m. on the fourth day after the patient was admitted, an order was written to start a 0.2 mg/hour HYDROmorphone infusion with 0.2mg HYDROmorphone for breakthrough pain every 30 minutes prn. The original order did not include the route of administration. The pharmacy processed the order as subcutaneous route of administration, which was reflected on the pharmacy computer generated MAR (Medication Administration Record). The patient was started on a HYDROmorphone pump at 3:30 p.m. that day. At 6:30 p.m. the patient was noted to be comfortable and sleeping. At 8:00 p.m. the patient was noted to have reduced level of consciousness and over the course of the night remained rousable only when stimulated. At 6:20 a.m. the next morning the patient was found without vital signs.

Upon reviewing the orders for the patient, the nursing staff noted a discrepancy between the order of 0.2 mg/hr HYDROmorphone infusion, and the pump, which had been programmed to infuse 2 mg/hr of HYDROmorphone.

The Coroner's Committee identified four key issues:
1. Transcription error
2. Lack of independent double check processes for transcription , administration of high-alert medication and infusion pump programming
3. Infusion rate not included on the pharmacy-generated MAR
4. Selection and dosing of opioids in patients who are opioid-naive

SUMMARY:

This case involved the inadvertent administration of a ten-fold overdose of HYDROmorphone to a vulnerable elderly patient. Key contributing factors identified in this incident include a change in the opioid medication being administered from morphine to HYDROmorphone, and the subsequent transcription error that lead to the overdose. This case highlights the critical importance of including independent double checks in the medication use process. Opportunities for intervention to prevent and detect this and similar errors are present at every stage of the process – prescribing, order processing, dispensing, administration and monitoring — and require the involvement of all disciplines.

High-Risk Patients & High-Risk Medications

ENSURING SAFE AND EFFECTIVE THERAPY FOR PATIENTS

The Coroner has recommended that the Ontario College of Pharmacists educate clinicians on the definition of opioid tolerance, and review the patient conditions and comorbidities that may suggest the need for reduced dose of opioids.

ROLE OF THE PHARMACIST

Pharmacists are important members of the interdisciplinary team providing care to patients admitted to hospitals.[1] They are responsible for ensuring patients receive safe and effective drug therapy. This includes reviewing medications ordered before they are delivered to the nursing unit for appropriateness for the specific patient. Pharmacists must also collect and interpret relevant patient information, monitor the patient's response to medication, and document the care they have provided.[2] There are several steps in the medication review process that a pharmacist must take when a medication order is received — both in a hospital or community setting.

STEP 1: PRESCRIPTION REVIEW

Pharmacists have a responsibility to assess prescriptions to confirm they meet legal requirements, and to ensure the prescribed therapy is safe, effective and optimal for the patient.[2,3,4] There are three main components to assessing a prescription:

A. Review the medication

- Is it a high-alert medication[9] Does this medication require dose adjustments based on concomitant medical conditions or drug therapies?
- Does this medication have a narrow therapeutic index?
- Is this medication likely to cause clinically significant drug interactions when prescribed concomitantly with other medications?
- Are additional safeguards necessary to consider with this medication?

B. Review patient information (from patient profile and dialogue with the patient)

- Information gathered from the patient profile and through dialogue with the patient should be used to determine if the medication prescribed is appropriate for the patient as ordered.
- Patient demographics (individual characteristics of the patient) – i.e. age, weight, height, gender, allergies, high-risk patient population
- Clinical information – i.e. reason for admission, current medical conditions, renal function, liver function, laboratory values (i.e. WBC, Hgb, electrolytes etc.)

C. Complete a therapeutic check

- Is the dose both safe and appropriate based on patient information?
- Is the medication compatible with current medical conditions and allergies?
- Is the medication compatible with other medications the patient is taking?
- Is the prescription appropriate for this patient and the condition being treated?

If the mediation is not appropriate as ordered, it is the pharmacist's responsibility to appropriately act on this information.[2]

STEP 2: LABELLING OF PATIENT SPECIFIC MEDICATION AND TECHNICAL CHECK

Legislative requirements describe what is required on a prescription label.[3] Requirements depend on the medication, dosage form and route of administration.[4,5,6,14]

When deciding what to include on the label for a particular product or delivery device, a pharmacist must be sure sufficient information is provided to ensure the medication will be administered as intended. Information should be presented in a format that is easily understood and does not cause confusion for those who will be administering the medication. Once the medication has been selected, labelled, and verified against the original prescription, the product is sent to the hospital ward.

Things to consider including when preparing a label for a prescription:

- Patient's name, hospital ID number, location
- Generic name(s) of the drug
- Strength and quantity of ingredients
- Final concentration of active ingredients and base solutions/diluents
- Dosage form
- Total amount/volume of final product (in circumstances where overfill is required, the overfill volume should be printed on the label separate from the dose information)
- Rate of infusion/duration of infusion
- Beyond use date of the compound
- Manufacturer identification and lot number or pharmacy control number
- Storage conditions, if applicable
- Auxiliary labels, if applicable
- Date dispensed
- Barcode, if applicable
- Name of the pharmacy or hospital

STEP 3: PATIENT MONITORING

Pharmacists are responsible for monitoring medication therapy to ensure patient-specific medications are effective and safe.[2,7] This is particularly important for high-risk patient populations, when high-risk medications have been prescribed, or when the patient's condition is changing or unstable. Pharmacists should work to establish a method to identify and prioritize patient's who require follow-up, and the timeframe within which that should occur.[1,2]

STEP 4: DOCUMENTATION:

Documentation is a key element of every health professional's Standards of Practice and one of the most basic professional responsibilities.[8] Pharmacists are expected to document directly in the patient's healthcare record.[2,4,8] Relevant information should also be documented in the pharmacy system to support continuity of care and ensure other pharmacists who may also be providing care for that patient are informed of pertinent details regarding the patient's care plan.

Documentation may include:[8]

- Assessments, interventions, and recommendations where professional judgment was exercised
- Evidence on which the recommendations are based
- A follow-up plan that is sufficiently detailed to monitor the patient's progress and ensure continuity of care by the pharmacist, and other regulated health professionals or caregivers, if applicable
- Decision-making process

OPIOID TOLERANT PATIENTS:

The use of opioid therapy to manage pain is commonly seen in both acute and chronic care. Opioids are considered high-alert medications and require extra vigilance by pharmacists when they are prescribed.[9] High-alert medications are drugs that bear a heightened risk of causing significant patient harm, where the consequences of an error are much more serious in nature and can significantly impact patients.[9]

When receiving a prescription to increase the dose of an opioid, the pharmacist should identify it as a

high-alert medication and determine if the new dose prescribed is appropriate, given the total daily dose the patient received over the last 24 to 48 hrs. If the prescription is for a different opioid, or different route for the same opioid, the total 24-hour dose should be used to determine the equivalent dose.[16] However, it must be noted that any conversion is an estimate, and dosing on the lower end of the conversion dosing range is recommended.[10]

Appropriate opioid dosing will vary depending on whether a patient is considered opioid naïve or has developed tolerance following continued opioid use. Opioid tolerant patients are less susceptible to the effects of opioids in terms of pain relief and most side effects, (such as sedation and respiratory depression). However, no tolerance develops to the side effect of constipation.[15] According to the FDA definition, opioid tolerant patients are defined as patients who are taking, for one week or longer, at least:

- 60 mg oral morphine/day
- 25 µg transdermal fentanyl/hour
- 30 mg oral oxycodone/day
- 8 mg oral hydromorphone/day
- 25 mg oral oxymorphone/day
- An equianalgesic dose of any other opioid

OPIOID NAÏVE PATIENTS

Opioid naïve patients should be monitored closely not only for pain relief (efficacy) but also for constipation, sedation and respiratory depression (side effects).

HIGH-RISK PATIENT POPULATIONS:

Pharmacists need to consider each patient individually when reviewing medication orders to determine if therapy is safe and effective given the patient's unique circumstances. Elderly patients are considered high-risk patients not only because of age-related physiological changes (e.g. decreased renal function, changes in absorption etc.) but because they are often on many medications due to multiple chronic conditions which increases the risk of drug interactions.

Pediatric patients are also considered high-risk.[11] Factors that put pediatric patients at an increased risk for adverse drug reactions are:

- Different and changing pharmacokinetic parameters between patients at various ages and stages of maturational development
- Need for calculation of individualized doses based on the patient's age, weight, (mg/kg), body surface area (mg/m2) and clinical condition
- Lack of available dosage form and connections available for administration to neonates, infants and children
- Lack of stability, compatibility, or bioavailability data for extemporaneously compounded dosage formulations
- Need for precise dose measurement and appropriate drug delivery systems
- Lack of published information or Food and Drug Administration- approved labeling regarding dosing, pharmacokinetics, safety, efficacy ad clinical use of drugs in the pediatric population.

Other examples of patients that may be considered high-risk are those whose condition is unstable, have compromised organ function, or are at risk of clinically significant adverse drug reactions etc.

SUMMARY:

Pharmacy practice in Ontario is continuing to evolve, with pharmacists responsible for an even further expanded scope of practice. Doing nothing is no longer an option. OCP's Professional Responsibility Principles,[13] and Code of Ethics, along with the Standards of Practice, outline professional and ethical responsibilities when delivering patient care. Pharmacy professionals must use heightened caution and extra diligence when they encounter red flag situations, such as those that involve high risk drugs or vulnerable patient populations.

THIS CASE HIGHLIGHTS AT LEAST FOUR RED FLAGS:

1. Elderly patient (high-risk population therefore require greater scrutiny of patient-specific information including current medications)
2. High-alert medications (though not inherently more likely to cause medication errors, these carry an elevated risk of more serious harm if an error occurs with their use and so additional safeguards are required)[9]
3. Opioid naïve patient (switching to a high potency opioid-hydromorphone in an opioid naïve patient who was taking only low doses of morphine)
4. Change in route, schedule, and increased total daily dose
   - Conversion for dose equivalency between two different medications based on total daily dose
   - Conversion from one administration route (intermittent IV to a different route (continuous SC)
   - Conversion from intermittent prn dosing to continuous dosing

Pharmacy professionals must realize that a decision to do nothing is still a decision, and that you are professionally responsible and accountable for all decisions made when delivering patient care. Pharmacists must apply therapeutic judgment in order to assess the appropriateness of therapy given individual patient circumstances and must, when necessary, act appropriately to ensure that therapy is safe and effective. Pc

REFERENCES

1. Essential Medicines and Health Products Information Portal: A World Health Organization resource. Accessed online March 31, 2016 http://apps.who.int/medicinedocs/en/d/Jh2995e/2.2.html
2. NAPRA Model Standards of Practice 2009. Accessed online March 31, 2016 http://napra.ca/Content_Files/Files/Model_Standards_of_Prac_for_Cdn_Pharm_March09_Final_b.pdf
3. Drug and Pharmacies Regulation Act, R.S.O. 1990, c. H.4 s. 156
4. Accreditation Canada Qmentum Medication Management Standards 2017
5. ISMP Canada Epidural Safety Checklist 2015
6. OCP Guidelines for Compounding Preparations September 2006
7. Pharmacy Act S.O. 1991, c 36 s.3 (Scope of Practice)
8. OCP Documentation Guidelines 2012
9. Ontario Critical Incident Learning High Alert Medications: ISMP, January 2016, Issue 15..
10. Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain: Practice Toolkit. http://national-paincentre.mcmaster.ca/documents/practicetoolkit.pdf
11. ISMP USA Acute Care ISMP Medication Safety Alert Guidelines for preventing medication errors in pediatrics (from the The Journal of Pediatric Pharmacology and Therapeutics 2001;6:426-42) accessed online March 31, 2016 at (https://www.ismp.org/newsletters/acutecare/articles/20020601.asp).
12. Cipolle,J., Strand, L., Morley,P., Pharmaceutical Care Practice. 3rd Ed Chapter 8
13. OCP Professional Responsibility Principles
14. CSHP Compounding: Guidelines for Pharmacists 2014
15. http://www.medscape.com/viewarticle/733067_2
16. PL Detail-Document, Opioid Conversion Algorithm. Pharmacist's Letter/Prescriber's Letter. August 2012

PRACTICE TIP!

When thinking about narcotics reconciliation, manual and computer records are not error proof – while helpful, they can provide incomplete or incorrect data.
http://www.ocpinfo.com/practice-education/practice-tools/fact-sheets/recon-security/

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