



27-APR-1998-1060

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

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11/16/98

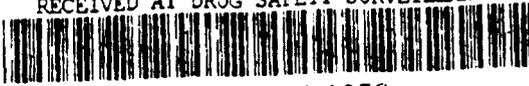
A Use onl

| A. Patient information                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                         |                                                 |                                   | C. Suspect medication(s)                                                                                                                                                                                        |  |                                                                                                  |  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------|-------------------------------------------------|-----------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|--------------------------------------------------------------------------------------------------|--|
| 1. Patient identifier<br>In confidence                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 2. Age at time of event:<br>or 33 yrs<br>Date of birth: | 3. Sex<br>(X) female<br>( ) male                | 4. Weight<br>unk lbs<br>or<br>kgs | 1. Name (give labeled strength & mfr/labeler, if known)<br>#1 TYLENOL Analgesic Unknown<br>#2                                                                                                                   |  |                                                                                                  |  |
| B. Adverse event or product problem                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                         |                                                 |                                   | 2. Dose, frequency & route used<br>#1 "often took 15 in 24 hrs"<br>#2                                                                                                                                           |  |                                                                                                  |  |
| 1. X Adverse event and/or Product problem (e.g., defects/mafunctions)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                         |                                                 |                                   | 3. Therapy dates (if unknown, give duration) from/to (or best estimate)<br>#1 starting around 11/97<br>#2                                                                                                       |  |                                                                                                  |  |
| 2. Outcomes attributed to adverse event (check all that apply)<br>( ) death (mo/day/yr)<br>( ) life-threatening<br>(X) hospitalization - initial or prolonged<br>( ) disability<br>( ) congenital anomaly<br>( ) required intervention to prevent permanent impairment/damage<br>(X) other: recovered                                                                                                                                                                                                                                                                                                             |                                                         |                                                 |                                   | 4. Diagnosis for use (indication)<br>#1 shoulder pain<br>#2                                                                                                                                                     |  |                                                                                                  |  |
| 3. Date of event<br>(mo./day/yr) 2/9/98                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                         | 4. Date of this report<br>(mo./day/yr) 04/15/98 |                                   | 5. Event abated after use stopped or dose reduced<br>#1 ( ) Yes ( ) No (X) N/<br>#2 ( ) Yes ( ) No ( ) N/                                                                                                       |  | 6. Lot # (if known)<br>#1 Unknown<br>#2                                                          |  |
| 5. Describe event or problem<br>Physician report of LIVER DAMAGE and OVERDOSE of an unknown TYLENOL® acetaminophen product in a 33 y/o female patient. Reportedly around November, the patient started taking Tylenol about 5 of 7 days, often taking 15 in 24 hrs. On 2/9/98, her husband found her face down on her bed, dazed (STUPOR) and shaking (TREMOR), eyes rolling back in her head. Patient was admitted to hospital and reportedly her liver was destroyed. Patient received three-fourths of a liver on 2/21/98. Ten days after transplant, she was discharged. No further information was provided. |                                                         |                                                 |                                   | 7. Exp. date (if known)<br>#1 Unknown<br>#2                                                                                                                                                                     |  | 8. Event reappeared after reintroduction<br>#1 ( ) Yes ( ) No (X) N/<br>#2 ( ) Yes ( ) No ( ) N/ |  |
| 6. Relevant tests/laboratory data, including dates<br>unknown                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                         |                                                 |                                   | 9. NDC # - for product problems only (if known)                                                                                                                                                                 |  |                                                                                                  |  |
| 7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)<br>shoulder pain for months                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                         |                                                 |                                   | 10. Concomitant medical products and therapy dates (exclude treatment of event)<br>unknown                                                                                                                      |  |                                                                                                  |  |
| G. All manufacturers                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                         |                                                 |                                   |                                                                                                                                                                                                                 |  |                                                                                                  |  |
| 1. Contact office - name/address (& mfring site for devices)<br>McNeil Consumer Products Company<br>Medical Affairs<br>7050 Camp Hill Road<br>Ft. Washington, PA 19034                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                         |                                                 |                                   | 2. Phone number<br>215-233-7820                                                                                                                                                                                 |  |                                                                                                  |  |
| 4. Date received by manufacturer (mo./day/yr) 04/10/98                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                         |                                                 |                                   | 3. Report source (check all that apply)<br>( ) foreign<br>( ) study<br>( ) literature<br>( ) consumer<br>(X) health professional<br>( ) user facility<br>( ) company represent<br>( ) distributor<br>( ) other: |  |                                                                                                  |  |
| 6. If IND, protocol #                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                         |                                                 |                                   | 5. (A) NDA # 17-552<br>IND #<br>PLA #<br>pre-1938 ( ) Yes<br>OTC product (X) Yes                                                                                                                                |  |                                                                                                  |  |
| 7. Type of report (check all that apply)<br>( ) 6-day (X) 15-day<br>( ) 10-day ( ) periodic<br>(X) initial ( ) follow-up #                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                         |                                                 |                                   | 8. Adverse event term(s)<br>OVERDOSE LIVER DAMAGE<br>STUPOR TREMOR                                                                                                                                              |  |                                                                                                  |  |
| 9. Mfr. report number<br>0965820A                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                         |                                                 |                                   | E. Initial reporter                                                                                                                                                                                             |  |                                                                                                  |  |
| 1. Health professional?<br>(X) Yes ( ) No                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                         |                                                 |                                   | 2. Occupation<br>physician                                                                                                                                                                                      |  | 3. Initial reporter also sent report to FDA<br>( ) Yes ( ) No (X) U/                             |  |



Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event

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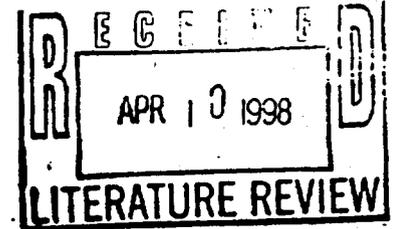


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LEVEL 1 - 7 OF 10 STOI

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THE ORANGE COUNTY REGISTER

March 3, 1998 Tuesday MORNING EDITION



SECTION: NEWS; Pg. A01

LENGTH: 853 words

HEADLINE: Mom has transplant in Tylenol overdose;  
 MEDICINE: The Santa Ana woman receives a new liver after taking too much medication for shqlder pain.

BYLINE: MICHELLE NICOLosi, The Orange County Register

## BODY:

Ingrid Anderson's shoulder had been hurting for months, but the busy Santa Ana mother of three didn't have time to go to the doctor.

Instead, she took Tylenol anytime the pain became bad.

Lots of Tylenol.

Starting around November, Anderson megadosed the over-the-counter painkiller about five of seven days. She often took 15 in 24 hours \_ twice the recommended amount.

Anderson's husband, Jim, found her face down Feb. 9 on her bed, dazed and shaking, eyes rolling back in her head.

Anderson's liver had been destroyed by the acetaminophen. Without a transplant, she would die within the week, doctors predicted.

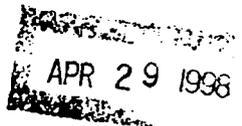
"You just don't realize," said Anderson, who received her transplant Feb. 21 and went home Monday. "You think, 'It's over the counter. It's OK. ' "

At least 60 people are rushed to Orange County hospitals every year with acetaminophen poisoning. Only the most severe cases need a transplant, said Dr. David Imagawa, director of UCI's Liver Transplant Program.

Anderson's is the first acetaminophen-related liver transplant done at UCI.

"I've learned my lesson," Anderson said. "You gotta be aware of what you're doing, or you can harm yourself. "

Anderson repeated the safety message again and again to TV and newspaper reporters. Her children \_ Peter, 9; Joseph, 7; and Kristina, 3 \_ smiled for the cameras. Anderson's father filmed the





27-APR-1998-1061

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Individual Safety Report



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tumult.

Anderson vowed to "never take another minute for granted." She said that God gave her a second chance so she could warn others about the dangers of abusing over-the-counter medication.

Anderson is alive in part because of recent changes in the rules governing how transplant livers are given out.

Under the old rules, which gave livers first to those with chronic disease, she would have been fifth or sixth in line. She probably would have died waiting, Imagawa said. About 7,200 people in the United States are waiting for a liver transplant, but only about 3,900 received one last year because of the shortage of donor organs.

But the new rules allow patients with sudden acute onset of the disease, like Anderson, to go to the head of the line. When a liver became available Feb. 21, her doctors took a helicopter in the predawn hours to San Bernardino to harvest the organ.

As surgeons were working to prepare the liver, an urgent call came in at 8 a.m. from the University of California, Los Angeles.

"They said, 'We have a young baby, the transplant liver (he'd received earlier) has failed. We need another liver, right now!'" Imagawa said.

Could the baby have part of the liver slated for Anderson?

The liver is the only organ that regenerates itself. Anderson received three-fourths of a liver, but it will be whole again within two months, Imagawa said.

The patient and her doctors agreed, and another group of surgeons flew from UCLA to resect part of the donor liver for infant Eduardo Limos, who is now doing well.

Meanwhile, Imagawa was busy removing Anderson's liver. He finished about 3 p.m., just as the new liver arrived.

"Perfect timing," Imagawa said.

The transplant went so smoothly because UCLA, UCI and Cedars-Sinai are part of a liver-transplant team that has worked together for years, Imagawa said.

The three groups have helped more patients by splitting livers 40 times over the past few years, but have never had to do it before in an emergency situation, Imagawa said.

If the systems hadn't already been in place for the hospitals to work together, the baby might have died, he said.

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Imagawa's final word of warning: Labels se

Obey them.

"It's when we try to outsmart medicine that you get into trouble," he said.

Symptoms of overdose include jaundice \_ yellow skin and eyes \_ nausea and fatigue. If you suspect an overdose, call the Poison Control Center at (800) 876-4766.

#### CHART LIST WHAT YOU SHOULD DO

The Food and Drug Administration has a special warning for anyone who regularly has three or more alcoholic drinks a day: Check with a doctor before taking aspirin, Tylenol or any other over-the-counter painkiller.

The FDA said Friday that it wants to put that warning on every bottle of nonprescription pain pills, citing risks of stomach bleeding or liver damage.

Some pain pills, including Tylenol, already voluntarily carry certain alcohol warnings. The danger made headlines in 1994, when a Virginia man won an \$ 8 million lawsuit claiming he needed a liver transplant after mixing Tylenol and his habit of wine with dinner.

In November, the government proposed warnings that anyone who drinks three or more alcoholic beverages a day should ask a doctor before taking:

Acetaminophen, sold under the brand name Tylenol and other names, because alcohol use might increase the risk of liver damage.

Aspirin.

Ibuprofen, the active ingredient in Advil and other brands.

Ketoprofen, the active ingredient in Orudis KT and Actron.

Naproxen sodium, the active ingredient in Aleve, because alcohol use might increase the risk of stomach bleeding.

GRAPHIC: BLACK & WHITE PHOTO; CHART; HEALTHY; Ingrid Anderson hugs her sons Joseph, 7, left, and Peter, 9, in her room at UCI Medical Center following a transplant.; CHART LIST - WHAT YOU SHOULD DO (SEE END OF TEXT)

LANGUAGE: ENGLISH

LOAD-DATE: March 09, 1998

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TUESDAY, MARCH 3, 1998



# Mom has transplant in Tylenol overdose

**MEDICINE:** The Santa Ana woman receives a new liver after taking too much medication for shoulder pain.

By MICHELLE MCCLOSKEY  
The Orange County Register

Ingrid Anderson's shoulder had been hurting for months, but the busy Santa Ana mother of three didn't have time to go to the doctor.

Instead, she took Tylenol anytime the pain became bad.

Lots of Tylenol.

Starting around November, Anderson megadosed the over-the-counter painkiller about five of seven days. She often took 13 in 24 hours — twice the recommended amount.

Anderson's husband, Jim, found her face down Feb. 9 on her bed, dazed and shaking, eyes rolling back in her head.

Anderson's liver had been destroyed by the acetaminophen. Without a transplant, she would die within the week, doctors predicted.

"You just don't realize," said Anderson, who received her transplant Feb. 21 and went home Monday. "You think, 'It's over the counter. It's OK.'"

At least 60 people are rushed to Orange County hospitals every year with acetaminophen poisoning. Only the most severe cases need a transplant, said Dr. David Imagozwa, director of OCH's Liver Transplant Program.

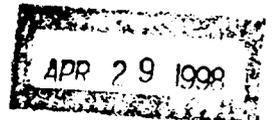
Anderson's is the first acetaminophen-related liver transplant done at UCI.

"I've learned my lesson," Anderson said. "You gotta be aware of what you're doing, or you can harm yourself."

Anderson repeated the safety message again and again to TV and newspaper reporters. Her children — Peter, 9; Joseph, 7; and Kristina, 3 — smiled for the cameras. Anderson's father filmed the result.

Anderson vowed to "never take another minute for granted." She said that God gave her a second chance so she could warn others about the dangers of abusing over-the-counter medication.

Please see LIVES Page 3





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The Orange County Register FROM PAGE 1 Wednesday, March 8, 1998

NEWS 5

# LIVER: Mom undergoes transplant

**FROM 1**  
Anderson to allow in part because of cancer changes in the rules governing how transplant organs are given out.

Under the old rules, which gave livers first to those with chronic disease, she would have been fifth or sixth in line. She probably would have died waiting, Imbruglia said. About 7,200 people in the United States are waiting for a liver transplant. But only about 1,000 received one last year because of the shortage of donor organs.

That the new rules allow patients with sudden liver onset of the disease, like Anderson, to go to the head of the line. When a liver became available Feb. 22, her doctors took a helicopter to the pancreas bank to retrieve the organ to harvest the organ.

As surgeons were working to prepare the liver, an urgent call came in at 8 a.m. from the Uni-



**HEALTHY:** Ingrid Anderson hugs her sons Joseph, 7, left, and Peter, 8, in her room at UC Medical Center following a transplant.

**SHANE GARDNER**  
The Register

versity of California, Los Angeles. "They said, 'We have a young baby, the transplant (your son's received earlier) has failed. We need another liver, right now!'" Imbruglia said.

Could the baby have part of the liver stored for Anderson?

The liver is the only organ that regenerates itself. Anderson received three-fourths of a liver, but it will be whole again within two months, Imbruglia said.

The patient and her doctors agreed, and another group of surgeons flew from UCLA to remove part of the donor liver for infant Eduardo Lizaso, who is now doing well.

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The transplant went well.

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The three groups have helped spare patients by splitting livers to run over the past few years, but have never had to do it before in an emergency situation, Imbruglia said.

If the systems hadn't already been in place for the hospitals to work together, the baby might have died, he said.

Imbruglia's final word of warning: Labels are critical for a reason. Check them.

"It's when we try to get correct medicine that you get into trouble," he said.

Signs of overdose include jaundice — yellow skin and eyes — nausea and fatigue. If you suspect an overdose, call the Poison Control Center at (800) 676-7462.

## WHAT YOU SHOULD DO

The Food and Drug Administration has a special warning for anyone who regularly has fever or more stomach pain. A shot of Tylenol or any other over-the-counter painkiller.

The FDA said Friday that it wants to get that warning on every bottle of over-the-counter pain pills, along with other stomach bleeding or liver damage.

Some pain pills, including Tylenol, already carry a warning about stomach bleeding. The danger could be even worse in 1998, when a Virginia man took an 80 pill bottle claiming he needed a liver transplant after taking Tylenol and his hole of vomit with dinner.

It's important, the government proposed warning that anyone who takes more or more stomach pain pills a day should call a doctor before using.

• **Acetaminophen**, also under the brand name Tylenol and other names, because alcohol use might increase the risk of liver damage.

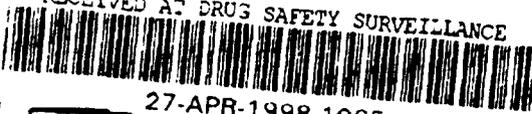
• **Aspirin**.

• **Supplements**, the same ingredients in Advil and other brands.

• **Supplements**, the same ingredients in OTC and Advil.

• **Supplements**, the same ingredients in Advil, because alcohol use might increase the risk of stomach bleeding.

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## Transplant Process

The liver is the body's largest internal organ and performs several critical functions. A malfunctioning or diseased liver can cause severe illness, even death. A new transplantation procedure allows doctors to save two livers with one liver. Three teams of doctors are required for such a procedure:



1 Teams 1 and 2 remove old livers from patients, usually one adult and one infant

2 Team 2 removes donor liver and divides the organ for transplantation

3 Patients receive partial transplants of donor liver, doctors sew into place

## About the Liver

The cone-shaped red-brown organ functions as the body's chemical factory and regulates chemistry in blood.

Some fast facts:

- Weighs 2.5 to 3.5 pounds
- Produces important proteins for blood plasma, including albumin and cholesterol
- Regulates blood level of amino acids
- Cleans the blood of drugs and poisonous substances
- Up to three-fourths of the liver cells can be destroyed or surgically removed before the organ ceases to function
- Partial liver transplants will grow and regenerate

Note: Follow-up includes two to three weeks of hospitalization, up to six months for recovery

# ONE LIVER, DOUBLE BLESSING

### Transplant a Gift of Life for Woman and Infant

By MARCIDA DODSON  
Times Staff Writer

**O**RANGE—Ingrid Anderson needed a new liver, fast. But when a donor liver became available, Anderson's doctor had an unexpected request: Would she give part of the organ to a baby who also needed a transplant?

"When I heard it was a baby, that was all I had to hear," said Anderson, who agreed immediately to the split-liver procedure.

"I have three children. If I can survive on three-quarters of a liver and help a baby who needs a liver, there's no



KEVIN P. GIBBY / Los Angeles Times

"I feel blessed. I was able to get a new liver and able to help a young baby too."

**INGRID ANDERSON**  
Left, with son Pedro, 3, and her husband, Dr. Ricardo Lopez

question."

On Monday, Anderson, 33, was checking out of UCI Medical Center in Orange, 10 days after receiving the larger portion of a liver from a 19-year-old trauma victim in San Bernardino. The baby recipient, 7-month-old Ricardo Lopez of North Hollywood, is recovering well at UCLA Medical Center, said his mother, Cynthia Ramos.

While this was not the first time UCI and UCLA doctors have done the procedure, the split-liver transplant is still a relatively new development that helps alleviate the critical shortage of donor organs, said Dr. David K. Inagawa, chief of UCI's transplantation division.

"It's two for one, if you will," he said. The concept of splitting a liver from a

Please see LIVER, B3

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TEL: 714 4565505

# LIVER: Woman, Infant Share Gift of Life

Conditioned from an endow developed after doctors began transplanting parts of livers from living relatives into children, which is still a new area, Imagawa said. Doctors found that both donor and recipients recovered well.

Because liver tissue is the same throughout the organ, a donor liver can be split for transplant into one small child and one baby, who needs a small organ anyway, he said. Liver tissue regenerates, he said. Anderson's liver should be normal size in a few months, while the baby's liver will grow with him, he said.

The risks are minimal, Imagawa said. The chief concern is "the plumbing," he said—cutting the blood vessels into and out of the organ so that both pieces can be connected to the vessels in the recipients. But the donor liver must be perfect, or it compromises the success of both recipients, he said.

The liver received by Anderson and Ricardo was the 40th split and transplanted as part of a three-hospital program composed of UCI, UCLA and Cedars-Sinai. Anderson was the 10th UCI patient to receive a split liver, about 25 adults at UCLA and five at Cedars-Sinai have received the others. All 40 babies receiving the partial livers have been at UCLA.

Split-liver transplants require three teams of doctors, Imagawa said: one for the donor, and one for each of the two recipients.

Anderson was the first recipient at UCI to receive one in an emergency.

Anderson, 23, of Santa Ana suffered from acute acetaminophen poisoning, the result of inadvertently taking too much acetaminophen pain reliever in too short a time. She had been taking the medication, she said, because of chronic shoulder pain.

"A kind of gas with motherhood," she said from her hospital bed. "I didn't take time to take care of myself. It was easier to take some pills than to do what I needed to do—have it checked out."

Her husband, Jim, could not wake her on the morning of Feb. 2. Paramedics rushed her to Coastal Community Hospital in Santa Ana, and two days later she was transferred to UCI Medical Center.

Imagawa said that 50% of acute acetaminophen poisoning cases are treated without a transplant. But Anderson was not responding to treatment. After a week, he placed her on the transplant list. Most people waiting for a liver suffer from chronic disease and wait for months, but emergency cases go to

the top of the list, he said. Without a transplant, Anderson had no more than three or four days to live, he said.

Within 48 hours, the transplant team learned of the liver in San Bernardino. Then Imagawa received a call from UCLA. Could Anderson's transplant be delayed several hours, long enough for UCLA to send someone to San Bernardino to bring back part of the organ for a baby? Imagawa said yes, then asked Anderson if she would agree.

"There was no doubt," Anderson said. "I feel blessed. I was able to get a new liver and able to help a young baby too."

Ramona, baby Ricardo's mother, said the procedure was the second liver transplant for her son, who hadiliary, strain, a congenital malformation of the bile ducts. The first liver came from another baby, but the surgery was not successful because Ricardo developed a clot in the vein afterward. The second transplant has taken well, she said.

On Wednesday, a beaming Anderson said she felt "on top of the world" as she hugged her children, praised her "dream team" doctors and told all who would listen about the success of taking over-the-counter medicine without following the label directions.

But almost everyone does it, Imagawa said. "We have a bad headache, and we figure that if the label says take two, we can take three," he said. But acetaminophen is toxic to liver cells, he said, and must be taken within carefully determined limits. Any consumption of alcoholic beverages while taking the drug can cause further damage.

In Anderson's case, he said, though she had not been drinking, there appeared to have been some built-up toxicity from repeated, frequent usage of acetaminophen, culminating with a high dosage—16 tablets within 24 hours.

"I learned the hard way," Anderson said, her eyes filling with tears as she recalled that at one point, doctors told her husband to prepare the children—Peter, 2, Je-

seph, 7, and Kristina, 3—for the possibility "that mommy won't be coming home."

Surrounded by cards and hand-drawn get-well wishes from her children's classmates, she vowed Monday that she will take better care of herself.

She has a busy schedule of volunteering in her children's classrooms, helping out at the family's two freight businesses and taking care of three small children. But now she has a different perspective, she said.

"It's not the quantity of things I do, it's the quality. I can always get the other things done tomorrow," she said. "But if I don't take care of myself, I won't be there to take care of my kids."



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