Background: Data on iatrogenic diseases (IDs) have been recorded for the past 25 years. We determined whether aging of the general population and medical advances, including more powerful drugs and complex procedures, have altered the incidence, causes, and consequences of severe IDs during this period.

Methods: One-year retrospective study was conducted in an adult medical-surgical intensive care unit (ICU) affiliated with a French general hospital in an area of 200,000 inhabitants. All the patients admitted to the ICU during 1994 were screened for IDs. Patients with community or hospital-acquired IDs on admission were included. Follow-up assessed morbidity, mortality, workload, and costs of care for IDs, and the rate of preventable IDs.

Results: Of 623 patients admitted to the ICU, 68 (10.9%) were included; the cause of the ID was drugs in 41, medical acts in 12, and surgical acts in 15. These 68 patients were in the ICU for 472 days, with a 13% fatality rate (9 patients) and a financial cost of US $688,470. They were not different from the 555 other ICU patients in terms of severity, mortality, workload, and length of stay in the ICU. Risk factors for ID were old age and the number of prescribed drugs. The rate of preventable ID was 51%.

Conclusions: Iatrogenic diseases are a persistent and important reason for admission to the ICU, and the risk factors, causes, and consequences remain unchanged since 1980. Despite 25 years of experience with high-technology medicine, ID still has a negative impact on the health and resources of society.

Arch Intern Med. 1999;159:71-78

There have been numerous North American and European studies on iatrogenic diseases (IDs) during the past 3 decades. Although the incidence of community-acquired ID is not precisely known, it seems to account for 2% to 10% of outpatient consultations and 3% to 7% of hospital admissions, most of them (95%) after drug exposures. These patients spend 8 to 10 days in the hospital and have a fatality rate of 2% to 6% and a rate of preventable events of 50%. The elderly are most at risk. Hospital-acquired ID occurs in 2% to 36% of hospitalized patients and can be caused by drug-induced illness or events after medical and surgical procedures (35%–75% of cases). Hospital-acquired ID increases the length of stay and has a fatality rate of 3.7% to 14.0% and a permanent disability rate of 6.5%. The rate of preventable events is 20% to 50%. Once again, the elderly are more at risk, but the severity of the underlying diseases, the number of prescribed drugs, and the pattern and location of care are also factors. The risk of ID is high in neurologic, thoracic, vascular, and cardiac surgery units; intensive care units (ICUs); emergency departments; and interventional radiology because the association of severe coexisting diseases and the complexity of treatment are likely to lead to iatrogenic events.

Severity is closely linked to the nature of the adverse event and the underlying medical condition. Iatrogenic complications are life-threatening in 10% to 26% of cases. Trunet et al found that ID accounted for 12.6% of admissions in the ICU, with a fatality rate of 20.0%, in an adult medicosurgical ICU affiliated with a French tertiary care university hospital.

Most of the studies published during the past 25 years have shown the negative effects of ID on population health, the cost of medical care, and the rate of malpractice claims. Health care providers have reacted by developing quality-of-care initiatives, including better identification of ID and determination of risk factors.
PATIENTS AND METHODS

STUDY POPULATION

This study was conducted in the 15-bed medicsurgical ICU (MSICU) affiliated with the 500-bed General Hospital at Compiegne, France. Cardiac surgery, neurosurgery, and organ transplantation are not performed in this institution. In addition to the MSICU, a 6-bed cardiac care unit takes care of patients with cardiovascular emergencies in the absence of other severe organ failure. Admission to the MSICU of any patient with at least 1 life-threatening organ failure or metabolic disorder, or requiring emergency dialysis or mechanical ventilation, is authorized by 1 of the permanent or on-duty MSICU senior physicians after discussion with the physician (emergency department, operating room, or wards) caring for the patient. All the patients admitted to the MSICU between January 1, 1994, and December 31, 1994, were retrospectively screened for ID as the purpose of admission to the unit. Screening was performed by house staff composed of 3 board-certified anesthesiologists (B.D., E.L.M., E.B.), 1 cardiology and internal medicine board-certified intensivist (Y.D.), and 1 resident (B.F.). Each patient was identified as having ID or not by consensus, and the causes, relationship between prescription or procedure and ID, preventability, and severity of the iatrogenic events were determined. If consensus was not obtained, the patient was not included. Each assessment was made according to the following criteria and definitions.

DEFINITIONS

Iatrogenic disease was defined as a disease induced by a drug prescribed by a physician; or after a medical or surgical procedure, excluding intentional overdose, nonmedical intervention; or unauthorized prescription, and environmental events (falls, equipment defect).

Adverse event was defined as an unintended and noxious event caused by medical management carried out according to the best of medical science.

Preventable event was defined as an event that should not occur if management is the best that medical science can provide.

Nosocomial infection was defined as a localized or systemic infection, occurring at least 48 hours after hospital admission, that was not present or incubating at the time of admission. Nosocomial infection was defined as an infection after medical or surgical management, whether or not the patient was hospitalized.

RELATIONSHIP BETWEEN PRESCRIPTION OR PROCEDURE AND IATROGENIC DISEASE

Drug-Induced Disease

We used the progressive criteria of Karch and Lasagna. The relationship between a drug and an adverse reaction was divided into the following 5 levels: definite: a reaction that follows a reasonable temporal sequence from administration of the drug, or in which the drug level has been established in body fluids or tissues, that follows a known response pattern to the suspected drug, and that is confirmed by dechallenge and rechallenge; probable: a reaction that follows a reasonable temporal sequence from administration, that follows a known response pattern to the suspected drug, that is confirmed by dechallenge, and that could not be reasonably explained by the patient's condition; possible: a reaction that follows a reasonable temporal sequence from administration and that follows a known response pattern to the suspected drug, but that could have been produced by the patient's clinical condition or other therapy given to the patient; conditional: a reaction that follows a reasonable temporal sequence from administration...
and that does not follow a known response pattern to the suspected drug, but that could not be reasonably explained by the known characteristics of the patient's clinical condition; and doubtful: any reaction that does not meet the above criteria.

**Disease After Medical or Surgical Procedure**

As there is no standard definition, we used the same criteria as Trunet et al. The relationship was good if the following 4 criteria were all satisfied; otherwise the relationship was conditional: the complication is known and recorded in the medical literature; it is not reasonably explained by the patient's underlying diseases; there is a reasonable temporal sequence from the procedure to the complication; and a relationship can be established from anatomical criteria (such as colonic perforation linked to endoscopy), microbiologic criteria (such as urinary tract infection after urinary catheterization), or chemical criteria (such as radiocontrast and renal failure).

**SEVERITY**

The severity of the ID was classified as fatal, life-threatening, or moderate. A fatal event is a complication principally responsible for death. Life-threatening ID requires intensive care (mechanical ventilation, vasopressors, hemodialysis, cardiac catheterization or pacing, tube thoracostomy, surgery, etc.). Complication was judged to be moderate if only routine management and monitoring were needed.

**DATA COLLECTION**

The following data were recorded for each patient admitted to the ICU during the study period: age, sex, number of prescribed drugs before admission to the ICU, origin of patient (home or hospital), length of stay, number of prescribed drugs before admission to the ICU, origin of patient (home or hospital), length of stay, and outcome in the ICU. The Simplified Acute Physiology Score was calculated within 24 hours after admission to the ICU as an index of disease severity. The McCabe score (3 classes: fatal during hospitalization, ultimately fatal within 5 years, and not fatal) was used as an index of the severity of the underlying medical condition. The Omega score was calculated at the end of the patient's stay as an index of total workload (Figure). The Omega score system is an ICU-specific activity scoring system used in the French ICUs since 1990, validated by the French Health Department and the Société de Réanimation de Langue Française. It is highly correlated with the Nursing Research Project 1987 scoring system used in Canada. The Omega score is calculated by summing up 47 therapeutic interventions collected during each patient's ICU stay and scored from 1 to 10. For instance, tracheostomy is scored as 6 points per hospitalization; hemodialysis, 10 points per course; and mechanical ventilation, 10 points per day. We also recorded the nature and relationship between disease and procedure, and the severity and the preventability of disease for each patient with ID. The cost of care in the ICU was calculated by means of the global “day's fare” allocated to our ICU by the French care system, which was €8122 per day for 1994 (US $1300 per day).

**STATISTICAL ANALYSIS**

The characteristics of the patients are expressed as means ± SDs or as the number of patients or events. Comparisons between patients were made by Student t test for continuous variables and the χ² test with Yates correction when indicated for categorical variables. A P value of less than .05 was considered statistically significant. Data were stored on Microsoft EXCEL (Version 4.0; Microsoft Inc, Redmond, Wash), and all probability calculations were performed with SAS Macro software (SAS Institute Inc, Cary, NC).

Twelve patients were admitted for ID after a medical procedure (3 performed out of hospital). The relationship was good in all cases, and ID was preventable in 3 of the 12 cases. Symptoms were severe in 7 instances, resulting in death in 2 cases. Six patients had iatrogenic infections, among which 3 were nosocomial infections and 3 were community-acquired infections (tetanus, bacteremia after lower-limb venous sclerotherapy and urinary catheter).

Fifteen patients had surgical complications, all of which occurred in the operating theater, in the recovery room, or on surgical wards. The relationship was good in 14 of the 15 cases, and the complication was preventable in 2 instances. Symptoms were severe in 5 cases, leading to death in 1 patient.

Overall, these 68 admissions resulted in 472 days of hospitalization in the ICU, with a mean length of stay of 6.9 ± 9.3 days (range, 1-52 days). The workload required was 3612 Omega points, with a mean of 53 points per patient and a density rate of 7.7 points per day of hospitalization. The fatality rate in the ICU was 13% (9/68 patients). Cost of medical care in the ICU for these 68 patients was estimated at US $688,470.

About half (35/68) of these IDs were considered to be preventable. The 30 preventable events after drug-induced ID were caused by the use of inappropriate drugs in 6 cases, an error in dose in 8 cases, inadequate follow-up of therapy in 14 cases, and failure to use prophylactic treatment in 2 cases. Three events were linked to medical procedures (radiocontrast infusion in 2 and hemorrhoid sclerotherapy in 1). Two were caused by surgical procedures (suprapubic cystostomy tube and episiotomy). These 35 preventable IDs resulted in 189 days of hospitalization in the ICU and 5 deaths (14%). Cost of medical care in the ICU was evaluated at US $275,680, with a workload of 1434 Omega points (41 points per patient, 7.6 points per day).

The 623 patients admitted to the ICU during the study period were divided into group 1 (n = 555), patients without IDs; group 2 (n = 41), patients with drug-induced IDs; and group 3 (n = 27), patients with IDs after medical or surgical procedures (Table 5). Groups 2 and 3 were next compared individually with group 1.

**Table 5**

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of Patients</th>
<th>Number of Preventable IDs</th>
<th>Number of Nonpreventable IDs</th>
<th>Total Number of IDs</th>
<th>Total Workload</th>
<th>Total Omega Score</th>
<th>Total Cost of Medical Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>555</td>
<td>30</td>
<td>251</td>
<td>281</td>
<td>$275,680</td>
<td>1434</td>
<td>$688,470</td>
</tr>
<tr>
<td>2</td>
<td>41</td>
<td>20</td>
<td>21</td>
<td>41</td>
<td>$41,000</td>
<td>98</td>
<td>$688,470</td>
</tr>
<tr>
<td>3</td>
<td>27</td>
<td>15</td>
<td>12</td>
<td>27</td>
<td>$27,000</td>
<td>117</td>
<td>$688,470</td>
</tr>
</tbody>
</table>

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Score) or mortality. Likewise, patients who experienced
from group 1 with respect to workload in the ICU (Omega
in the ICU. Nevertheless, groups 2 and 3 did not differ
ratio (29 women and 12 men), a higher Simplified Acute
Group 2 patients were older and had an inverted sex ra-
computed tomographic.

Continuous Monitoring in the ICU
Mechanical Ventilation
Multiple Colostomies, or Enterostomies
Complex Surgical Dressing, Laparotomy,
Protective Isolation
Continuous Hemodiafiltration, Peritoneal Dialysis
Category 3
Transport Outside the ICU and/or Return to the Unit
Hemodialysis
Gastroscopy and Coloscopy
Bronchoscopy
Echography in the ICU
Angiography in the ICU
Category 2
Use of Fibrinolytic Drug
Use of Vasopressors
External Skeletal Traction
Tracheotomy
Gastroesophageal Varices Tamponade
Ureterostomy Tube
Temporary Cardiac Pacing
Arteriovenous Shunt
Continuous Intravenous Sedation:
Diagnostic Peritoneal Lavage
Massive Blood Transfusion (>50% Blood Mass)
Continuous Intravenous Sedation: ≥24 h
Arteriovenous Shunt
Temporary Cardiac Pacing
Ureterostomy Tube
Gastroesophageal Varices Tamponade
Tracheotomy
External Skeletal Traction
Treatment of Cardiac Arrest
Use of Vasopressors
Use of Fibrinolytic Drug

Total 1

Total 2

Total 3

ICR Omega = Total 1 + 2 + 3

Sample of tally sheet used for calculating the Omega score, an index of the
total workload for a patient's stay in the intensive care unit (ICU). ICR
indicates relative complexity index (the value of each act in terms of
workload); Nb, number of acts; Tot, total; CSF, cerebrospinal fluid; and CT,
computed tomographic.

Group 2 patients were older and had an inverted sex ra-
tio (29 women and 12 men), a higher Simplified Acute
Physiology Score, and more prescribed drugs on ad-
mision. Group 3 patients were also older and stayed longer
in the ICU. Nevertheless, groups 2 and 3 did not differ
from group 1 with respect to workload in the ICU (Omega
score) or mortality. Likewise, patients who experienced
adverse events were compared with those who experi-
enced preventable events (Table 6). The only factor in-
creasing the risk of preventable events was age. The lo-
dation of drug prescription (home or hospital) was not a
risk factor for drug-induced ID.

This study, conducted 15 years after the one by Trunet
et al,25 clearly confirms the persistence and the para-
mount importance of ID as a cause of admission to the
ICU. Trunet et al found that 12.6% of the ICU admis-
sions were linked to ID. The rate was 10.9% in the pre-
sent study, with the use of the same criteria and defini-
tions. There was also a high rate of preventable events,
accounting for 51% of the ID in our study, while Trunet
et al found 41%. The stability of these rates over this long
time is somewhat surprising, as a decrease might have
occurred because of better recognition, care, and pro-
phylaxis for ID or an increase because of more powerful
and/or invasive treatment for more sick and aged pa-
tients. The 2 trends may well have canceled each other
out.

We believe that this exhaustive review, although ret-
rospective, of all ICU charts and medical reports from the
623 patients admitted during 1994, done early in the fol-
lowing year by the permanent clinical team taking care
of these patients, provides a sensitive investigation. How-
ever, this advantage is probably outweighed by the method
of identification of ID, requiring unanimity of judgment
for a definitive inclusion. Although this procedure pro-
vided reliability of assessments, we believe that it led to
an underestimation of the number of included IDs.

The drugs implicated in ID remained standard.
Cardiovascular drugs accounted for 31%, anti-in-
fiammatory and analgesic drugs for 20%, and antibiot-
ic for 11% of cases of drug-induced ID. This has not
changed in 20 years,4,7 but there have been striking changes in each class of
drugs.

Angiotensin-converting enzyme inhibitors (alone or
associated with diuretics) are the leading class of cardio-
vascular drugs involved in ID, before diuretics and oral
anticoagulants, whereas digitalis compounds and older
antihypertensive drugs have almost disappeared. Few IDs
related to antiarrhythmic or thrombolytic drugs were en-
countered in this study, because of the presence of a 6-
bed cardiac care unit in the same hospital. Nonsteroidal
anti-inflammatory drugs emerged as the leading anti-
inflammatory and analgesic drugs causing iatrogenic
events, and there were no complications linked to cor-
ticosteroids or aspirin. These changes probably reflect
changes in prescription habits.

Trunet et al25 found 2 incompatible blood transfu-
sions among the 23 drug-induced IDs, whereas we ob-
served no complication linked to the transfusion of blood
products. The drastic vigilance guidelines regarding blood
products enforced in France in 1992 after the “contami-
nated blood products affair” have reduced the fre-
cuency of gross compatibility accidents.49 We also saw
no severe ID caused by antidiabetic drugs, perhaps as a
result of improved education of diabetic patients by the
endocrinological staff of our hospital. Finally, only 2 of

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the 41 patients with drug-induced ID had allergic reactions severe enough to require ICU admission. This recruitment bias explains the differences of distribution for drug-induced ID, when compared with out-of-hospital or ward studies.6,10,13,15,17

The 12 IDs caused by medical procedures included 6 severe infections, 3 of them hospital acquired (2 cases of bacteremia after peripheral venous catheterization and 1 after urinary tract catheterization). We could not assess the preventability of these catheter-related infections because we had no information about their real need and the adherence to aseptic guidelines for their insertion and care.

The preventability of an iatrogenic accident after surgery is often difficult to determine because the surgeon is both judge and judged. This probably lowers the ability to distinguish between an adverse event and a preventable event. The 2 surgical iatrogenic events defined

<table>
<thead>
<tr>
<th>No. of Patients</th>
<th>Type of Drug</th>
<th>Iatrogenic Illness (No.)</th>
<th>Severity (No.)†</th>
<th>Preventability, No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Diuretics alone</td>
<td>Hypokalemia (2), hyperkalemia (2)</td>
<td>M (2), LT (1), F (1)</td>
<td>2/4</td>
</tr>
<tr>
<td>1</td>
<td>ACEIs alone</td>
<td>Acute renal failure (1)</td>
<td>M (1)</td>
<td>1/1</td>
</tr>
<tr>
<td>3</td>
<td>ACEIs + diuretics</td>
<td>Hyperkalemia (1), dehydration (1), mesenteric infarction (1)</td>
<td>M (2), F (1)</td>
<td>3/3</td>
</tr>
<tr>
<td>3</td>
<td>Oral anticoagulants alone</td>
<td>Severe bleeding (3)</td>
<td>M (2), F (1)</td>
<td>3/3</td>
</tr>
<tr>
<td>3</td>
<td>Oral anticoagulants + interactive drug</td>
<td>Severe bleeding (3)</td>
<td>M (2), F (1)</td>
<td>3/3</td>
</tr>
<tr>
<td>5</td>
<td>NSAIDs alone</td>
<td>Gastrointestinal tract bleeding (4)</td>
<td>M (4)</td>
<td>2/4</td>
</tr>
<tr>
<td>6</td>
<td>Anesthesia</td>
<td>Cardiac failure (2), respiratory failure (3)</td>
<td>M (4), LT (1)</td>
<td>3/5</td>
</tr>
<tr>
<td>5</td>
<td>Intravenous fluid infusion</td>
<td>Fluid overload (4), hemodilution (1)</td>
<td>M (4), LT (1)</td>
<td>5/5</td>
</tr>
<tr>
<td>2</td>
<td>Amiodarone</td>
<td>Pneumonitis (2)</td>
<td>M (1), F (1)</td>
<td>0/2</td>
</tr>
<tr>
<td>2</td>
<td>Antibiotics</td>
<td>Hepatitis (1), allergic skin reaction (1)</td>
<td>M (2)</td>
<td>1/2</td>
</tr>
<tr>
<td>2</td>
<td>Cytotoxic drugs</td>
<td>Acute renal failure (1), aplastic marrow (1)</td>
<td>LT (1), F (1)</td>
<td>1/2</td>
</tr>
<tr>
<td>7</td>
<td>Miscellaneous‡</td>
<td>Coma (1), metabolic disorders (4), respiratory failure (1), serum sickness (1)</td>
<td>M (6), LT (1)</td>
<td>6/7</td>
</tr>
</tbody>
</table>

*ACEI indicates angiotensin-converting enzyme inhibitor; NSAID, nonsteroidal anti-inflammatory drug.
†M indicates moderate; LT, life-threatening; and F, fatal.
‡Including potassium and calcium oral therapies, digitalis, neuroleptics, theophylline, β-blockers, and influenza vaccine.

<table>
<thead>
<tr>
<th>No. of Patients</th>
<th>Type of Procedure</th>
<th>Iatrogenic Illness (No.)</th>
<th>Severity (No.)*</th>
<th>Preventability, No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Radiocontrast infusion in patients with renal failure</td>
<td>Acute renal failure (2)</td>
<td>M (1), LT (1)</td>
<td>2/2</td>
</tr>
<tr>
<td>3</td>
<td>Radiotherapy</td>
<td>Radiation enteritis (2), acute myeloblastic leukemia (1)</td>
<td>M (2), LT (1)</td>
<td>0/3</td>
</tr>
<tr>
<td>2</td>
<td>Peripheral venous catheterization</td>
<td>Bacteremia (2)</td>
<td>M (1), LT (1)</td>
<td>0/2</td>
</tr>
<tr>
<td>2</td>
<td>Urinary tract catheterization</td>
<td>Urinary tract infection with bacteria (2)</td>
<td>LT (1), F (1)</td>
<td>0/2</td>
</tr>
<tr>
<td>1</td>
<td>Lower-limb venous sclerotherapy</td>
<td>Bacteremia (1)</td>
<td>M (1)</td>
<td>0/1</td>
</tr>
<tr>
<td>1</td>
<td>Hemorrhoidal sclerotherapy</td>
<td>Generalized tetanus (1)</td>
<td>LT (1)</td>
<td>1/1</td>
</tr>
<tr>
<td>1</td>
<td>Cardiac catheterization</td>
<td>Ventricular arrhythmia (1)</td>
<td>F (1)</td>
<td>0/1</td>
</tr>
</tbody>
</table>

* M indicates moderate; LT, life-threatening; and F, fatal.

<table>
<thead>
<tr>
<th>No. of Patients</th>
<th>Type of Procedure (No.)</th>
<th>Iatrogenic Illness (No.)</th>
<th>Severity (No.)*</th>
<th>Preventability, No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Colonic surgery</td>
<td>Colonic anastomotic leakage (2)</td>
<td>M (2)</td>
<td>0/2</td>
</tr>
<tr>
<td>3</td>
<td>Abdominal (2), and orthopedic (1) surgery</td>
<td>Thromboembolism (3)</td>
<td>M (2), LT (1)</td>
<td>0/3</td>
</tr>
<tr>
<td>3</td>
<td>Endoscopy (2) and peritoneoscopy (1)</td>
<td>Bladder (1), large-bowel (1), gallbladder (1) perforations</td>
<td>M (1), LT (1), F (1)</td>
<td>0/3</td>
</tr>
<tr>
<td>1</td>
<td>Aortobifemoral graft</td>
<td>Rectal ischemia (1)</td>
<td>LT (1)</td>
<td>0/1</td>
</tr>
<tr>
<td>2</td>
<td>Subphrenic (1) and cervical (1) surgery</td>
<td>Pneumothorax (2)</td>
<td>M (2)</td>
<td>0/2</td>
</tr>
<tr>
<td>1</td>
<td>Suprapubic cystotomy tube</td>
<td>Bladder rupture (1)</td>
<td>M (1)</td>
<td>1/1</td>
</tr>
<tr>
<td>1</td>
<td>Total hip arthroplasty</td>
<td>Nonhemorrhagic shock (1)</td>
<td>M (1)</td>
<td>0/1</td>
</tr>
<tr>
<td>1</td>
<td>Epistaxis tamponade</td>
<td>Acute laryngeal obstruction (1)</td>
<td>LT (1)</td>
<td>1/1</td>
</tr>
<tr>
<td>1</td>
<td>Abdominal surgery</td>
<td>Postoperative hypoxemia (1)</td>
<td>M (1)</td>
<td>0/1</td>
</tr>
</tbody>
</table>

* M indicates moderate; LT, life-threatening; and F, fatal.
as preventable included (1) a laborious attempt at suprapubic cystotomy drainage, without previous echographic verification of the bladder repletion, leading to a bladder laceration, and (2) a mispositioned nasopharyngeal balloon tamponade (inflated through the larynx) for active epistaxis, which was followed by acute respiratory distress. These 2 procedures were performed by residents, with a delayed call to senior staff because of the disaster.

The overall fatality rate of patients with ID was 13% (9/68 patients), not significantly different (χ² = 0.55; P > .50) from the 17% fatality rate of the patients admitted to the ICU for other reasons (93/555). The fatality rate in the study by Trunet et al²⁵ was 19.5% (not significantly different from our study [χ² = 0.76; P > .50]).

The risk factors identified herein are the same as in earlier studies⁶,¹⁰,¹¹,¹³,¹⁷,¹⁸: old age (probably mainly women in our country) and the number of drugs prescribed before admission.¹³,¹⁴,²³ Drug-induced iatrogenic events, and particularly the preventable ones, are as likely to occur at home as in the hospital.

We distinguished preventable iatrogenic events from adverse events because the implications for responsibility of physicians are obviously quite different. An adverse event is an unexpected, unavoidable deleterious event after a medical prescription or procedure. That is preventable iatrogenic event. A preventable event is an event that could have been avoided if the medical act or prescription had respected the state of the art of medical science. The 51% rate of preventable events (35/68 patients) found in our study agrees with the results of others.¹⁰,¹₄-₁₆,₂₅,₃₂,₅₁ This high rate results in part from biased recruitment to the ICU, as the severity of iatrogenic disease seems to be correlated with errors.¹⁴ The immediate causes of preventable ID recorded are unremarkable: dosage error, contraindication or drug interaction unawareness, prophylaxis or monitoring omission, and technical error. However,

**Table 4. The 55 Drugs Involved in Iatrogenic Diseases**

<table>
<thead>
<tr>
<th>Type of Drug</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretics</td>
<td>7 (13)</td>
</tr>
<tr>
<td>Oral anticoagulants</td>
<td>6 (11)</td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatory drugs</td>
<td>6 (11)</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>6 (11)</td>
</tr>
<tr>
<td>Anesthesia</td>
<td>5 (9)</td>
</tr>
<tr>
<td>Intravenous fluid infusion</td>
<td>5 (9)</td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitors</td>
<td>4 (7)</td>
</tr>
<tr>
<td>Miscellaneous*</td>
<td>16 (29)</td>
</tr>
</tbody>
</table>

*Includes influenza vaccine, amiodarone, cyclic antidepressants, oral calcium and potassium therapies, theophylline, digitals, neuroleptics, cytotoxic drugs, β-blockers, and corticosteroidal anti-inflammatory drugs.

**Table 5. Characteristics of Patients With Iatrogenic Disease After Drug Exposure and After Medical and Surgical Procedures, and the Noniatrogenic Patients*  

<table>
<thead>
<tr>
<th></th>
<th>Noniatrogenic Patients (n = 555)</th>
<th>Drug Exposure (n = 41)</th>
<th>Medical and Surgical Procedures (n = 27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD, y</td>
<td>53.1 ± 20.0</td>
<td>70.8 ± 17.0</td>
<td>64.8 ± 17.0</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>322:233</td>
<td>12.29</td>
<td>15:12</td>
</tr>
<tr>
<td>SAPS, mean ± SD</td>
<td>11.1 ± 7.0</td>
<td>14.1 ± 5.0</td>
<td>12.5 ± 8.0</td>
</tr>
<tr>
<td>McCabe score, No. of patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatal or ultimately fatal within 5 y</td>
<td>198</td>
<td>18</td>
<td>9</td>
</tr>
<tr>
<td>Nonfatal</td>
<td>357</td>
<td>23</td>
<td>18</td>
</tr>
<tr>
<td>Omega score, mean ± SD</td>
<td>55 ± 86</td>
<td>32 ± 35</td>
<td>96 ± 124</td>
</tr>
<tr>
<td>No. of drugs before admission, mean ± SD</td>
<td>2.1 ± 2.2</td>
<td>4.0 ± 2.6</td>
<td>2.1 ± 2.2</td>
</tr>
<tr>
<td>Length of stay in ICU, mean ± SD, d</td>
<td>6.0 ± 7.5</td>
<td>4.3 ± 2.9</td>
<td>9.3 ± 13.7</td>
</tr>
<tr>
<td>No. of deaths</td>
<td>93</td>
<td>6</td>
<td>3</td>
</tr>
</tbody>
</table>

*Includes influenza vaccine, amiodarone, cyclic antidepressants, oral calcium and potassium therapies, theophylline, digitals, neuroleptics, cytotoxic drugs, β-blockers, and corticosteroidal anti-inflammatory drugs.

**Table 6. Comparison of Patients Having Adverse Effects and Those With Preventable Events**

<table>
<thead>
<tr>
<th></th>
<th>Adverse Effects (n = 33)</th>
<th>Preventable Events (n = 35)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD, y</td>
<td>62.7 ± 14.0</td>
<td>75.7 ± 17.0</td>
<td>.001</td>
</tr>
<tr>
<td>Sex, M/F</td>
<td>17:16</td>
<td>11:24</td>
<td>.03</td>
</tr>
<tr>
<td>SAPS, mean ± SD</td>
<td>14.1 ± 7.0</td>
<td>12.3 ± 6.0</td>
<td>.26</td>
</tr>
<tr>
<td>McCabe score, No. of patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatal or ultimately fatal within 5 y</td>
<td>11</td>
<td>16</td>
<td>.88</td>
</tr>
<tr>
<td>Nonfatal</td>
<td>12</td>
<td>19</td>
<td>.58</td>
</tr>
<tr>
<td>Omega score, mean ± SD</td>
<td>51.0 ± 51.0</td>
<td>37.5 ± 130.0</td>
<td>.59</td>
</tr>
<tr>
<td>Length of stay in ICU, mean ± SD, d</td>
<td>6.3 ± 5.7</td>
<td>5.0 ± 12.5</td>
<td>.59</td>
</tr>
<tr>
<td>No. of drugs in drug-related diseases, mean ± SD</td>
<td>3.6 ± 2.1</td>
<td>4.4 ± 2.6</td>
<td>.17</td>
</tr>
<tr>
<td>Location of drug exposure before admission, No.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home</td>
<td>6</td>
<td>18</td>
<td>.75</td>
</tr>
<tr>
<td>Hospital</td>
<td>5</td>
<td>12</td>
<td>.79</td>
</tr>
<tr>
<td>No. of deaths</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

*SAPS indicates Simplified Acute Physiology Score; ICU, intensive care unit.
the in-depth underlying causes of human fallibility and malpractice leading to these mishaps are worth examining. There are 3 types of error: error resulting from ignorance, negligence, or misjudgment.

Errors caused by ignorance (2 of 35 errors in this study) might be illustrated by a physician who does not recognize an unusual disease or does not perform exceptional care, although he or she took attentive care of the patient according to the best of his or her own knowledge. Such errors are probably difficult to avoid as the complexity and field of medical knowledge increase.

Errors caused by negligence (22 of 35 errors in this study) include acts that are knowingly below acceptable standards, as are violations of aseptic guidelines or omission of allergy checking. This lack of rigor probably is prompted by multiple factors, such as exhaustion, business factors, and loss of motivation.

Couch et al \(^1\) \(^2\) originally identified 5 causes of medical misjudgment in surgery, easily transposable to any medical activity: (1) misplaced optimism, (2) unwarranted urgency, (3) an urge for perfection, (4) fashionable therapy, and (5) insufficient restraint and deliberation.

The cost of ID for these 68 patients in human (472 days in the ICU, 9 deaths) and financial (US $688 470) terms is probably underestimated. The financial costs were calculated by means of a daily set price calculated and revised each year by the hospital financial services. The morbidity, sequelae, and later morbidity attributable to ID after the survivors left the ICU were not followed up. If the present study group (68 patients per year per 200 000 inhabitants) is considered to be representative, extrapolation leads to 45 deaths, 2360 days of hospitalization in the ICU, and US $3.44 million per 1 million inhabitants per year. These amazing figures do not include IDs occurring in other high-risk units not present in our hospital and cases treated outside the ICU, at home, or unrecognized. Indirect iatrogenic events, such as crashes and occupational or domestic accidents experienced by patients who are prescribed psychotropic drugs, are also not recorded as IDs. The type of severe iatrogenic events investigated may well be only the tip of the ID iceberg.

We confirmed that ID is still a major cause of hospitalization in the ICU, accounting for 11% of admissions, half of which are preventable. The morbidity, mortality (13% in our study), and cost of ID are certainly biased by the design of this study (patients with ID severe enough to require treatment in the ICU). Nevertheless, the global impact of ID on the health and resources of society is probably underestimated. The challenge, in this era of high-technology medicine, is to better understand the in-depth underlying causes of errors, to reduce the incidence of preventable iatrogenic events. This could provide a better quality of care at a lower cost.

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REFERENCES

42. Burstin HR, Johnson WG, Lipsitz SR, Brennan TA. Do the poor sue more? a case-control study of malpractice claims and socioeconomic status. JAMA 1993;270:1697-1701.