

OPPORTUNISTIC INFECTIONS IN CHILEAN AUTOPSY CASES, 1960-1986¹

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INTRODUCTION

Infections produced by opportunistic agents have come to pose one of the most important problems of infectious pathology in developed countries, from both the diagnostic and therapeutic standpoints. Stimulated by the introduction and development of procedures and therapies that in one way or another prolong the lives of patients with deeply depressed defenses, the frequency of these infections has experienced a steady and well-documented increase since the 1940s (1-5). Today opportunistic infections, particularly mycotic infections, are also having an important impact in some Latin American countries (6-8). In our own country, isolated cases and small outbreaks of opportunistic infections have been reported; but although these appear to be on the rise, there is insufficient published data to document the trend (9-24).

Not only does this information gap exist, but many opportunistic infectious agents are morphologically

distinctive, and their morphologic demonstration in tissue is the conclusive diagnostic proof of infection. For these various reasons, since 1981 we have been applying the best morphologic techniques available (5, 25, 26) to autopsy material from patients who had been immunodepressed, debilitated, or predisposed in some way to develop opportunistic infections. Concurrently, and with the same techniques, we have retrospectively examined autopsy material available from past years back to 1960. The general purposes of this work have been as follows: (1) to determine the frequency of classic opportunistic infections in our autopsy material; (2) to find out how this frequency has changed in recent years; (3) to identify the predominant types of opportunistic infections in our material and the frequency of the various clinical-anatomic forms; and (4) to define the underlying conditions involved.

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MATERIALS AND METHODS

The retrospective study reported here examined all the available autopsies at the Catholic University Medical School's Department of Pathologic Anatomy from deaths occurring in 1960 through the first half of 1986, and also all the available autopsies at the Pathologic Anatomy Service of Santiago's San José Hospital (163 autopsies) dating from 1981 through 1985. A directed review was made of this histologic material in all cases where the clinical or morphologic diagnosis suggested a possible predisposition to development of opportunistic infection.

Naturally, the study was limited to opportunistic agents considered morphologically distinctive in tissues—these including fungi, members of the genus *Nocardia*, parasites, and viruses producing unusual cytopathic effects. Ordinary bacteria were disregarded because they are not sufficiently distinctive in histologic studies and cannot be classed as opportunistic on the basis of such studies alone.

The histologic material was stained with hematoxylin-eosin, periodic acid-Schiff (PAS) Gomori-Grocott, the McCallum-Goodpasture modification of the Gram stain, Kinyoun, and Mayer's mucicarmine. In cases involving viral infection, transmission electron microscopy was used to examine material recovered from paraffin. At the same time, the clinical data recorded for each case were obtained, including the record of treatments administered.

RESULTS

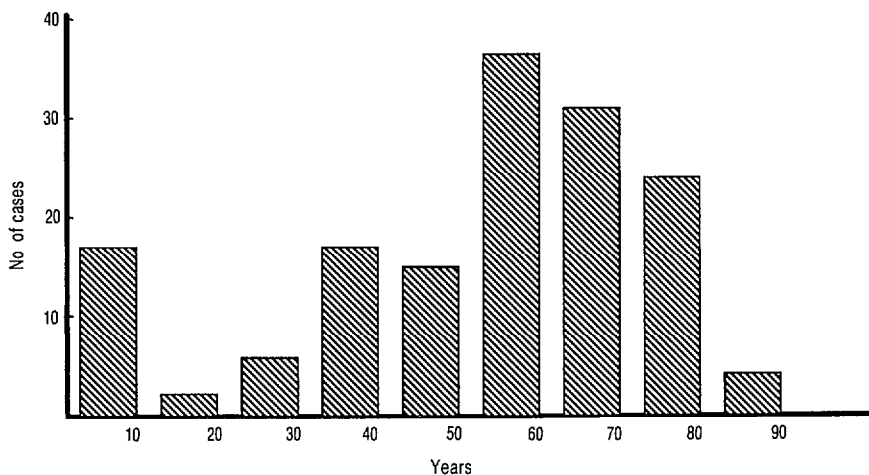
We examined material from a total of 5,612 autopsies—2,278 from 1960 through 1969, 1,676 from 1970 through 1979, and 1,658 from 1980 through mid-1986. Of these 5,612, 151 (2.7%) were found to have had opportunistic infections. In all, 175 such infections were detected, with 20 subjects being infected by more than one opportunistic agent. The types of agents responsible for these 175 infections were as follows: fungi, 72%; viruses, 23%; parasites, 3%; and *Nocardia*, 2%. Table 1 provides more specific information on these agents.

Regarding distribution by age and sex, 91 of the 151 autopsy subjects were men and 60 were women. As Figure 1 indicates, the subjects were concentrated in the sixth and seventh decades of life when they died, but one (a premature infant) had only 26 weeks of gestational age. At the other extreme, the eldest subject was a man 84 years old. The

TABLE 1. Opportunistic infections detected.

	Cases found	
	No.	(%)
<i>Fungal infections:</i>		
Candidiasis	71	(40.6)
Aspergillosis	41	(23.4)
Zygomycosis	10	(5.7)
Cryptococcosis	4	(2.3)
<i>Nocardia infections</i>	3	(1.7)
<i>Viral infections with:</i>		
Cytomegalovirus	19	(10.8)
Herpesvirus	18	(10.3)
Adenovirus	3	(1.7)
<i>Parasitic infections:</i>		
<i>Pneumocystis carinii</i> pneumonia	2	(1.1)
Strongyloidiasis	1	(0.6)
Isosporosis	1	(0.6)
Toxoplasmosis	1	(0.6)
Scabies	1	(0.6)

FIGURE 1. The ages of study subjects found to have opportunistic infections, by ten-year age groups.



average ages of subjects with certain specific opportunistic infections are shown in Table 2.

Figure 2 shows changes in the frequencies of the 175 opportunistic infections found during the study period. In the 1960–1969 period we found only 11 infections corresponding to 0.5% of the 2,278 autopsies studied. In the 1970–1979 period we found 38 infections corresponding to 1.8% of the 1,676 autopsies studied. And in the 1980–1986 period we found 126 infections corresponding to 6.6% of the 1,658 autopsies studied. As Figure 2 in-

FIGURE 2. Numbers of opportunistic infections (out of a total of 175) found among 2,278 autopsies in 1960–1969, 1,676 autopsies in 1970–1979, and 1,658 autopsies in 1980–1986, showing the types of agents responsible.

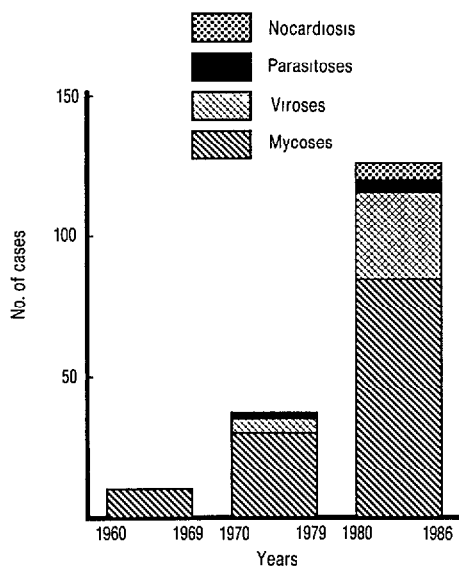


TABLE 2. Average age at death of study subjects with specific opportunistic infections.

Infection	Average age of study subjects
Nocardiosis	72 years
Aspergillosis	57 years
Candidiasis	53 years
Zygomycosis	50 years
Herpesvirosis	47 years
Cryptococcosis	46 years
Cytomegalovirosis	29 years
Adenovirosis	4 months

dicates, the 1960–1969 material yielded some opportunistic mycoses (11 in 2,278 autopsies); but the frequency of these mycoses was much higher in the next decade (30 in 1,676 autopsies), and much higher still in the 1980–1986 period (85 in 1,658 autopsies). Opportunistic viral infections (six in number) emerged in our material during the 1970–1979 period, but the frequency of such infections was much greater in the 1980–1986 material (34 in 1,658 autopsies). Parasitic infections first emerged in the 1970–1979 period (there were two in the 1970–1979 autopsies and four in the 1980–1986 autopsies), while *Nocardia* infections first emerged in the 1980–1986 period (three were found in the 1,658 autopsies).

As previously noted, 163 of the autopsies studied from 1981–1985 came from the San José Hospital. Thirty (18.4%) of these showed opportunistic infections, as compared to 79 (7.1%) of the 1,117 autopsies from these years at the Catholic University's School of Medicine. Despite this noteworthy difference, the types of opportunistic infections found at the two institutions appeared similar, as did their general distributions.

Changes in the frequencies with which the various opportunistic mycoses were observed are shown in Figure 3. These data indicate an explosive growth of such infections beginning in 1980, with a downward trend in the last year studied. The frequencies with which the various opportunistic virus infections were detected in the 1975–1986 period are shown in Figure 4.

FIGURE 3. Variations in the numbers of opportunistic mycotic infections detected in the 5,612 autopsies between 1960 and mid-1986, by type of mycosis.

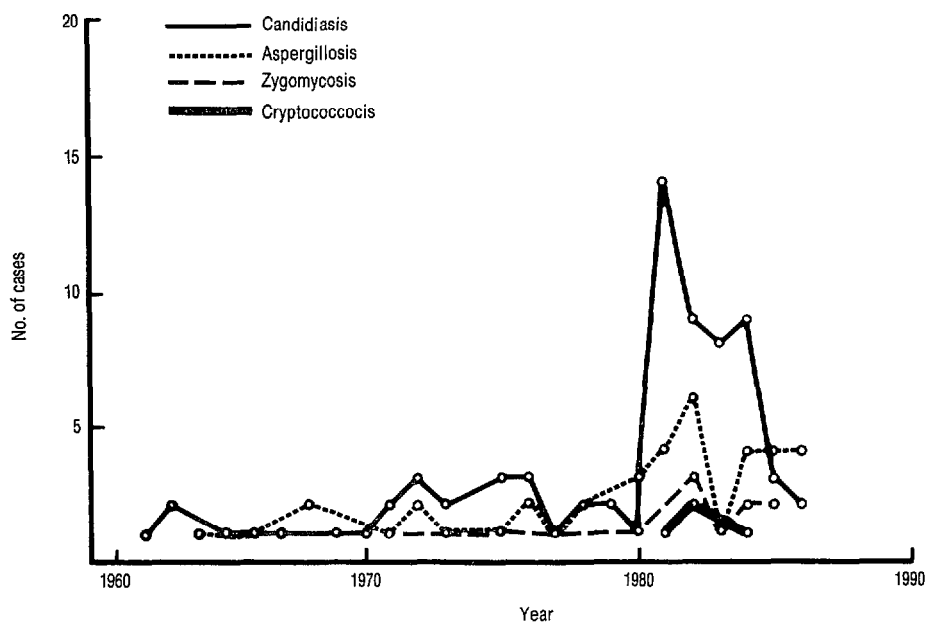
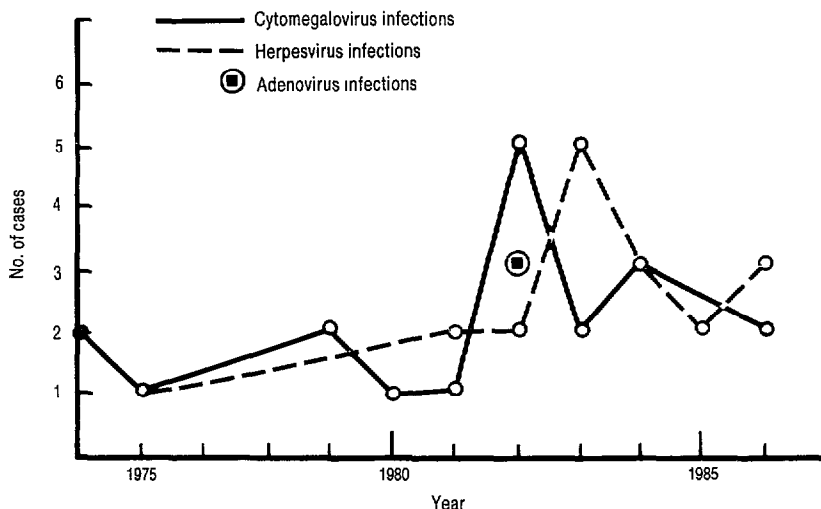


FIGURE 4. Variations in the numbers of opportunistic viral infections detected in the 5,612 autopsies between 1960 and mid-1986, by type of virus.



The dissemination of the mycotic and viral infections found, together with the organs or tissues involved in the case of localized infections, are shown in Table 3. Besides defining the areas invaded by these disease agents, we also sought to gauge the lethality of the different agents by constructing a rough lethality index—infections being regarded as lethal if they were broadly disseminated, or if they were deep and extensively compromised some vital organ. This index found 48% lethality for candidiasis, 88% for aspergillosis, 80% for zygomycosis, 94% for cytomegalovirus infections, and 70% for herpesvirus infections.

The organs compromised by the opportunistic infections detected, irrespective of the causative agents involved, are shown in Table 4.

Relationships between the 10 most frequently compromised organs and the opportunistic mycoses and nocardiosis are shown in Figure 5. The organ most frequently compromised in as-

pergillosis, zygomycosis, and nocardiosis was the lungs, while in candidiasis it was the esophagus and in cryptococcosis it was the brain.

Relationships between the same 10 organs and the various opportunistic viruses are shown in Figure 6. The organs most frequently compromised by cytomegalovirus were the lungs and intestines, while those most frequently compromised by herpesvirus were the esophagus, brain, skin, and lungs.

Underlying conditions predisposing patients to particular opportunistic infections were found for 171 of the 175 infections studied. These conditions are as shown in Table 5. Lymphohematologic disorders, the most frequent predisposing condition, included lymphomas being treated (12 cases), leukemias being treated (eight cases), agranulocytosis (five cases), myelomas being treated (two

TABLE 3. Clinical types of opportunistic mycotic and viral infections observed in tissues from the infected autopsy subjects.

	No. of cases
I. Mycoses:	
<i>Candidiasis</i>	71
Disseminated	30
Localized:	
Gastrointestinal mucosa	28
Respiratory mucosa	1
Vesical mucosa	1
Other mucosae	5
Lungs	5
Skin	1
<i>Aspergillus</i>	41
Disseminated	11
Localized:	
Invasive pulmonary forms	23
Noninvasive pulmonary forms	5
Cardiac	1
Gastric	1
<i>Zygomycosis</i>	10
Disseminated	3
Localized:	
Cranial	4
Invasive pulmonary	2
Noninvasive pulmonary	1
<i>Cryptococcosis</i>	4
Disseminated	1
Localized:	
Meningoencephalic	2
Lymphatic	1
II. Viral infections with:	
<i>Cytomegalovirus</i>	19
Disseminated	10
Localized:	
Pulmonary	8
Laryngeal	1
<i>Herpesvirus</i>	18
Disseminated	10
Localized:	
Glossopharyngoesophageal mucosa	5
Central nervous system	3
<i>Adenovirus</i>	3
Localized (lungs)	3

TABLE 4. Organs compromised by opportunistic agents detected in the 151 study subjects, by frequency of compromise.

Organ or tissue compromised	No. of cases
Lungs	104
Esophagus	51
Kidneys	29
Brain	26
Intestines	25
Stomach	22
Myocardium	21
Liver	19
Trachea	13
Skin	11
Spleen	10
Mouth and tongue	9
Meninges	8
Adrenal glands	8
Thyroid	8
Peritoneum	7
Main bronchus	6
Mediastinum	4
Nose and paranasal sinuses	3
Larynx	3
Pharynx	3
Endocardium	3
Large veins	3
Prostate	3
Urinary bladder	3
Hypophysis	2
Eye	2
Aorta	2
Pancreas	2
Pericardium	1
Peripheral artery	1
Bone marrow	1
Salivary gland	1
Ear	1
Bile duct	1

cases), myelofibrosis (one case), and malignant histiocytosis (one case). Of the 21 solid tumors, 20 were carcinomas and one was a sarcoma. The most frequent carcinomas were bronchial (in five cases), gastric (in two cases), colorectal (in two cases), pancreatic (in two cases), vesical (in two cases), and mammary (in two cases). The subjects involved had a history of immunodepressant chemother-

FIGURE 5. Organs and tissues found compromised by opportunistic mycotic and *Nocardia* infections, showing the general types of infectious agents detected.

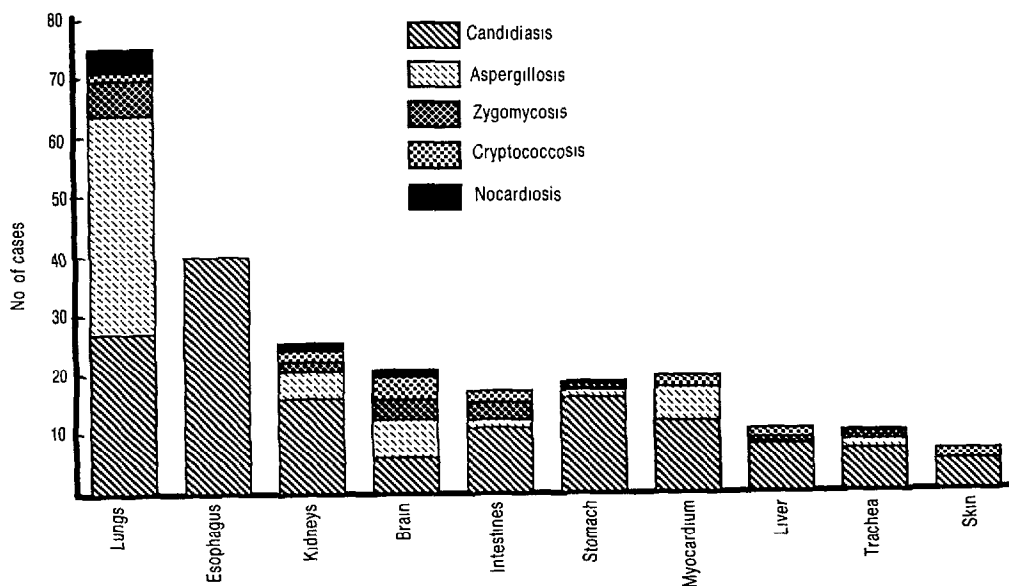


FIGURE 6. Organs and tissues found compromised by opportunistic viral infections, showing the general types of infectious agents detected.

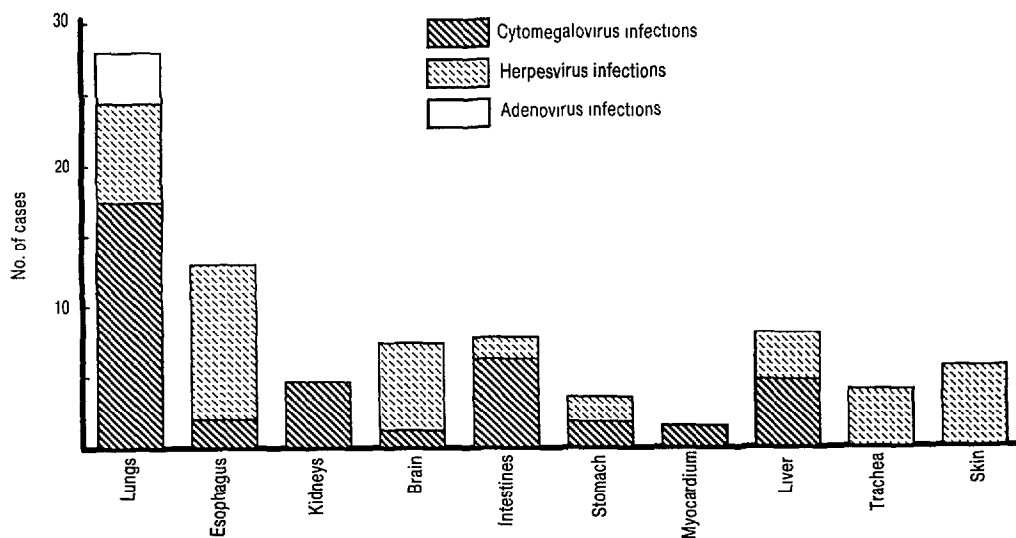


TABLE 5. Underlying conditions associated with the 175 observed opportunistic infections.

Underlying condition	No. of cases
Lymphohematologic disorders	29
Solid tumors	21
Diabetes mellitus	19
Abdominal surgery	15
Diffuse diseases of the connective tissue	12
Pulmonary tuberculosis	10
Kidney transplant	9
Prematurity	8
Senility	7
Bacterial infection + antibiotic therapy	7
Chronic renal insufficiency	6
Hepatic cirrhosis	6
Congenital immunodeficiency	6
Heart surgery	5
AIDS	4
Malnutrition	4
Anatomic disorders	2
Corticotherapy	1
Total	171

apy in 44 cases and of major surgery in 20 cases. This surgery was abdominal surgery in 15 cases and heart surgery in five.

Mixed opportunistic infections were found in material from 20 autopsies. Seventeen of these cases involved two agents, as follows: There were three cases of aspergillosis and candidiasis, three of aspergillosis and cytomegalovirus infection, three of candidiasis and cytomegalovirus infection, two of aspergillosis and zygomycosis, two of candidiasis and herpesvirus infection, one of aspergillosis and pneumocystosis, one of aspergillosis and herpesvirus infection, one of aspergillosis and nocardiosis, and one of zygomycosis and candidiasis. In two autopsies three agents were found, there being one case of aspergillosis, zygomycosis, and candidiasis, and one case of aspergillosis, pneumocystosis and cytomegalovirus infection. And in one au-

topsy (of an AIDS patient) four opportunistic infections were found—these being cryptococcosis, candidiasis, isosporiasis, and cytomegalovirus infection.

DISCUSSION AND CONCLUSIONS

The frequency with which opportunistic infections were found in our material rose around 1970 and rose sharply after 1980. Our finding of 6.6% opportunistic infections in the last period considered (1980–1986) is similar to that found by Aguirre et al. (27) for opportunistic mycoses in autopsy specimens at a general hospital in Mexico. Since this 6.6% figure would obviously rise if computed only for high-risk groups, our general situation would appear to resemble that described in other countries (1, 2, 6–8, 27–29). In this vein, it appears noteworthy that relatively few cases of pneumocystosis were found, despite our possession of the proper techniques for detecting this agent (25).

The most frequently occurring opportunistic infection found in our material was candidiasis; but it was not among the most lethal, these being cytomegalovirus infection, aspergillosis, zygomycosis, and herpesvirus infection.

The conditions predisposing subjects to opportunistic infections have been extensively discussed in the medical literature (1–3, 27–29). Virtually all of these, in nearly all their varied clinical-anatomic forms, were found in the histories of our study subjects.

In all of the cases studied, our diagnosis of opportunistic infection was based essentially on morphology—a circumstance underscoring the importance of using appropriate morphologic techniques to diagnose infections of this kind.

The findings reported here also demonstrate that classic opportunistic infections have become a frequent problem in our country that the clinician must suspect, diagnose, and treat—especially since advances in the treatment of infectious diseases have raised hopes for the victims of opportunistic agents (30).

SUMMARY

To help fill gaps in existing knowledge about opportunistic parasitic infections in Chile, histologic material from 5,612 autopsies performed from 1960 through mid-1986 was examined. This examination found 175 opportunistic agents in the tissues of 151 autopsy subjects—these agents including fungi (75%), viruses (23%), parasites (3%), and *Nocardia* (2%). Ordinary bacteria were disregarded because they are not sufficiently distinctive in histologic studies and cannot be classed as opportunistic on the basis of such studies alone. The most commonly found infections were candidiasis, aspergillosis, cytomegalovirus infection, herpesvirus infection, and zygomycosis.

The most commonly compromised organs and tissues were the lungs, esophagus, kidneys, brain, intestines, stomach, myocardium, liver, trachea, and skin. The more frequent primary underlying conditions predisposing subjects to opportunistic infections were lymphohematologic disorders, solid tumors, diabetes mellitus, major abdominal surgery, diffuse diseases of the connective tissue, pulmonary tuberculosis, kidney transplants, prematurity, and senility. In 44 cases the subject had a

history of immunodepressant chemotherapy. In general, the types of opportunistic infections, the clinical-anatomic forms of those infections, and the underlying conditions predisposing subjects to such infections appear to resemble those previously described in economically developed countries and in some other countries of Latin America.

The frequency of the opportunistic infections found rose markedly over time. During the 10 years from 1960 to 1969 we found only 11 cases in 2,278 autopsy subjects (0.5%); in the following decade we found 38 cases in 1,676 autopsy subjects (1.8%); and in 1980–1986 we found 126 cases in 1,658 autopsy subjects (6.6%). These findings point to a sizable increase of opportunistic infections in recent years.

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