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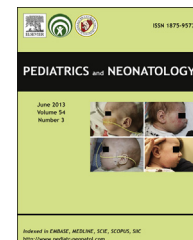
ORIGINAL ARTICLE

Nationwide Population-Based Epidemiologic Study of Childhood and Adulthood Intussusception in Taiwan

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Background: Most studies have evaluated the epidemiology of intussusception only in children. This was the first nationwide population-based study conducted to investigate the epidemiology and associated medical expenses of intussusception for all age groups in Taiwan.
Methods: Cases of intussusception were identified from the annual hospitalization discharge claims of the National Health Insurance Research Database with corresponding International Classification of Diseases, Ninth Revision (ICD-9) code 560.0, from January 2000 to December 2007.
Results: In total, 7255 incident cases of intussusception were detected. The majority of cases were children younger than 4 years of age. Significant male predominance was observed in the under-10-, 55–59-, and older-than-80-year age groups. The incidence peaked in the 1–2-year age group, reaching as high as 112.84 and 81.96 per 100,000 person-years for males and females, respectively. The incidence of intussusception was very low in adults. However, the medical expenses, number of coexisting neoplasms and malignancies, and hospitalization days were substantially higher in adults than in children. Although coexisting neoplasms developed in 40.8% of adult patients with intussusception, it occurred in only 0.4% of those younger than 3 years.
Conclusion: This study is the first to describe detailed age- and sex-specific incidence rates and medical expenses of intussusception for both pediatric and adult groups in Taiwan. There were significant differences between the two groups, with a much higher incidence in young children, but more coexisting neoplasms and malignancies and average medical expenses in adult patients.
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1. Introduction

Intussusception is the telescoping of a part of the intestine into itself. It is the most common cause of acute bowel obstruction in infants and small children.[1,2] If not diagnosed and treated promptly, reduced arterial blood supply may lead to bowel necrosis and perforation, causing peritonitis and even death.[1,3,4] In underdeveloped and developing countries, delay in the diagnosis and treatment is associated with high case-fatality rates, for example, 18% in Nigeria,[4] 20% in Indonesia,[5] and up to 54% in Ethiopia.[6]

Intussusception has attained public attention because of its association with the administration of the first licensed rotavirus vaccine, the reassortant rhesus-human tetravalent rotavirus vaccine (RRV-TV or Rotashield, Wyeth Lederle Vaccines, Philadelphia, PA, USA).[7,8] A new monovalent rotavirus vaccine has also been reported to be associated with a short-term risk of intussusception in approximately one of every 51,000—68,000 vaccinated infants in Mexico and Brazil.[9] Recent preliminary studies from Australia also suggest a link between the second-generation rotavirus vaccine RV5 and intussusception.[10]

In addition to occurring in children, bowel intussusception also occurs in adults, accounting for 5% of all cases of intussusception and 1—5% of those of bowel obstruction.[11] In Taiwan, the epidemiology of intussusception has been evaluated only in children,[12,13] with the highest recurrence and operation rates being observed in children under 1 year of age.[13] This study aimed to investigate the epidemiology and associated medical expenses of intussusception for both children and adults in Taiwan.

2. Materials and Methods

2.1. Data source

The compulsory National Health Insurance (NHI) program was launched in Taiwan on March 1, 1995, to provide comprehensive healthcare to all residents. The coverage rate of the NHI was 96.1% in 2000, which increased steadily to 98.6% in 2007.

In Taiwan, the National Health Insurance Research Database (NHIRD), a large computerized database derived from the NHI program by the Bureau of NHI and maintained by the National Health Research Institutes, has been made available to researchers since 2000 for study purposes. The data set used in this study consisted of de-identified secondary data, so that individual identifying information could not be accessed at any level. In order to use the NHIRD, we signed a written agreement stating that we had no intention of attempting to acquire information that could violate patients' privacy and that we would follow the Computer-Processed Personal Data Protection Law. The chairman of the Institutional Review Board of Changhua Christian Hospital confirmed that institutional review board approval was waived for this study.

2.2. Study participants

Cases of intussusception were retrieved from the hospitalization discharge claims of the NHIRD from January 2000 to December 2007, according to the discharge International Classification of Diseases, Ninth Revision (ICD-9) code 560.0, for patients of all ages. The data of the each hospitalization discharge claim contain a de-identified personal identification number, a date of birth, the length of hospitalization, the name of the relevant department, medical expenses, copayment, and the first five ICD-9 codes. The first episode of intussusception was used for calculating the disease incidence. Those who had the first three digits of coexisting ICD-9 codes 140—239 in any of the five discharge ICD-9 codes were regarded as having coexisting neoplasms. A coexisting malignancy was defined as having the first three digits of coexisting ICD-9 codes 140—208 in any of the five discharge ICD-9 codes. Adulthood was defined as age 20 years or above.

2.3. Statistical analysis

The incidence was calculated by dividing the number of new cases by the corresponding population size as published by the Ministry of Internal Affairs, Executive Yuan, Taiwan. Average age- and sex-specific incidences were calculated by dividing the number of new cases in each age and sex group by the age- and sex-specific population size, followed by averaging these data from 2000 to 2007. The population data for Taiwan were derived from the website of the Ministry of the Interior, Executive Yuan, Taiwan (http://www.moi.gov.tw/stat/english/year.asp). The average expense of inpatient service was calculated by dividing the sum of the expenses of inpatient services by the number of corresponding inpatient services.

Categorical data were analyzed with the chi-square test, and comparisons of continuous data from the two groups were performed with the independent t test. The p values of <0.05 from two-sided tests were considered statistically significant. All statistical analyses and graphing were performed using SPSS version 15.0 for Windows (SPSS, Inc., Chicago, IL, USA) and Microsoft Excel 2003.

3. Results

In total, 7255 patients with intussusception, including 2792 females, 4453 males, and 10 cases of unknown gender, utilized 8006 inpatient services during the study period. The majority (91.1%) of the patients were hospitalized only once. The annual sex-specific incidence rates of intussusception during 2000—2007 are shown in Table 1. The incidence rate was stable during the study period, ranging from 3.50 to 4.74 per 100,000 person-years, with an average incidence rate of 4.01 per 100,000 person-years. The average male/female incidence ratio was 1.59.

Age- and sex-specific incidence rates of every 5 years are shown in Table 2. Male predominance was obvious in patients younger than 10 years of age; however, in those older than 10 years of age, there was no significant male predominance except in the 55—59- and older-than-80-year groups. Most of the cases were young children, with 78.9% of cases occurring in those younger than 5 years of age and 83.1% in those younger than 10 years of age. Of the patients studied, 15.8% aged 20 years or older. The incidence was

Table 1   Incidence rate of intussusception in Taiwan.

	Total population (million)			New cases				Incidence rate per 10^5/y			M/F incidence ratio
	F	M	T	F	M	U	T	F	M	T	
2000	10.9	11.4	22.3	406	645	5	1056	3.73	5.66	4.74	1.52
2001	11.0	11.4	22.4	324	534	3	861	2.96	4.67	3.84	1.58
2002	11.0	11.5	22.5	400	578	0	978	3.62	5.03	4.34	1.39
2003	11.1	11.5	22.6	317	532	2	851	2.86	4.62	3.76	1.62
2004	11.1	11.5	22.7	352	562	0	914	3.16	4.87	4.03	1.54
2005	11.2	11.6	22.8	346	599	0	945	3.09	5.18	4.15	1.68
2006	11.3	11.6	22.9	333	468	0	801	2.95	4.04	3.50	1.37
2007	11.3	11.6	23.0	314	535	0	849	2.77	4.61	3.70	1.67

F = female; M = male; T = total; U = unknown gender; y = year.

very low in young and middle-aged adults, slightly increasing with old age for both sexes.

The averaged age-specific incidence rates of every 1 year in those younger than 10 years of age are detailed in Figure 1. The figure shows that the age-specific incidence peaked in the 1—2-year age group, reaching as high as 81.96 and 112.84 per 100,000 person-years for females and males, respectively; it then decreased rapidly with age.

The average medical expenses, hospitalization stay, and coexisting neoplasms and malignances among the different age groups are detailed in Table 3. In total, the average medical expense per inpatient service was 30,892 New Taiwan Dollars (TWD), the average copayment of each inpatient service was 1309 TWD, and the mean hospitalization stay was 4.88 days. However, there was substantial variation among the different age groups. Very few coexisting neoplasms or malignancies were observed in pediatric patients. Minimum medical expenses, least hospitalization stay, and a very small number of coexisting neoplasms and

malignancies were observed in the 1—3-year-old age group. However, substantially higher medical expenses, hospitalization days, and coexisting neoplasms and malignancies were reported in case of adults. Among the adult patients, 40.8% and 24.3% had coexisting neoplasms and malignancies, respectively. The rates of coexisting neoplasms and malignancies were especially high in the 60—80-year age group. The most common coexisting malignancy was colon cancer (ICD-9 code 153, 138 patients), followed by secondary malignant neoplasms of the respiratory and digestive systems (ICD-9 code 197, 61 patients) and malignant neoplasms of the small intestine including the duodenum (ICD-9 code 152, 46 patients).

4. Discussion

This study is the first to present detailed information on sex- and age-specific incidence rates of and medical

Table 2   Averaged age- and sex-specific incidence of intussusception.

Age group (y)	Case number					Averaged incidence per 10^5/y				
	F	M	U	T	Cumulative percentage	F	M	T	M/F incidence ratio	p
0—4	2175	3542	4	5721	78.9	45.0	67.1	56.6	1.5	<0.001
5—9	93	214	2	309	83.1	1.6	3.4	2.5	2.1	<0.001
10—14	21	21	0	42	83.7	0.3	0.3	0.3	0.9	n.s.
15—19	15	25	0	40	84.2	0.2	0.4	0.3	1.6	n.s.
20—24	26	38	1	65	85.1	0.4	0.5	0.4	1.4	n.s.
25—29	34	29	1	64	86.0	0.5	0.4	0.4	0.8	n.s.
30—34	21	36	1	58	86.8	0.3	0.5	0.4	1.7	n.s.
35—39	32	35	1	68	87.8	0.4	0.5	0.4	1.1	n.s.
40—44	34	42	0	76	88.8	0.5	0.5	0.5	1.2	n.s.
45—49	34	47	0	81	89.9	0.5	0.7	0.6	1.4	n.s.
50—54	37	41	0	78	91.0	0.6	0.7	0.7	1.1	n.s.
55—59	33	60	0	93	92.3	0.8	1.5	1.2	1.9	0.005
60—64	34	44	0	78	93.4	1.0	1.4	1.2	1.4	n.s.
65—69	40	50	0	90	94.6	1.4	1.9	1.6	1.3	n.s.
70—74	47	68	0	115	96.2	2.1	2.8	2.4	1.4	n.s.
75—79	49	70	0	119	97.8	3.0	3.6	3.3	1.2	n.s.
≥80	67	91	0	158	100.0	4.2	5.8	5.0	1.4	0.046

F = female; M = male; n.s. = not significant; T = total; U = unknown gender; y = year.
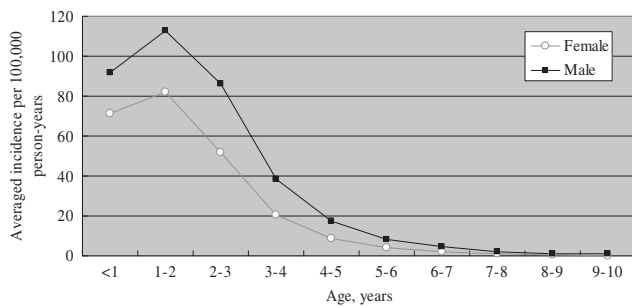
Figure 1 Averaged age-specific incidence of intussusception for those below 10 years of age.

expenses associated with intussusception for all age groups in Taiwan. With regard to the pediatric patients, our main results of male predominance and peak incidence at an age of 1—2 years are consistent with those of a previous study conducted in Taiwan during 1999—2001.[12] The incidence rate of intussusception was also stable during the entire study period (2000—2007). This reflects the quality of the data on annual discharge claims collected from the NHIRD as well as the stability of the disease.

The specific ICD-9 code for intussusception is 560.0. Because of its low incidence, it is difficult and impractical for an epidemiological approach to study the epidemiology of intussusception by field community studies. Therefore, the NHIRD is a good resource for studying the incidence of the disease.

The major limitation of the NHIRD is that the diagnosis relies on the ICD-9 code. The NHIRD lacks laboratory results and imaging studies. Despite this, we believe that the diagnosis of intussusception in this study was reliable for the following two reasons. First, the diagnostic tools for intussusception, including ultrasonography, abdominal plain film, and computed tomography, were widely available in Taiwan during the study period. Second, we enrolled only hospitalized cases, and the diagnosis was made after hospitalization, allowing for a thorough investigation. Because of the enrollment criteria, patients with intussusception who presented to an emergency department without hospitalization or to an outpatient clinic were not included. This may have caused underestimation of the incidence. Correlation with a prior or concurrent respiratory adenovirus infection has been noted in pediatric intussusception. There are 43 cases having coexisting diagnostic ICD-9 code 8.6 for enteritis due to specified virus. However, the number is probably underestimated because the virus isolation was not performed routinely and the virus isolation result was not available from the NHIRD.

The age-specific incidence of intussusception peaked in the 1—2-year age group, reaching 81.96 and 112.84 per 100,000 person-years for females and males, respectively. The peak incidence rates observed in Taiwan during our study were slightly higher than those reported in other regions, such as 60 per 100,000 in Singapore for patients under 2 years of age,[14] 65 per 100,000 in New Zealand,[15] 62 per 100,000 in the United States,[16] 66—75 per 100,000 in Europe,[17,18] and 78—100 per 100,000 in Hong Kong.[19] The differences in study results might have arisen due to the use of varied methodologies. Owing to the compulsory NHI, our data may reflect the true incidence more accurately.

The peak incidence of intussusception was observed in patients aged between 3 and 7 months in Singapore,[14] 6 and 9 months in Hong Kong,[19] and 5 and 7 months in the United States.[16] Both our study and a previous study in Taiwan[12] had consistent results in that the highest incidence of intussusception occurred between 12 and 24 months of age. The reason why Taiwanese children develop intussusception more frequently during the second year of life remains unclear. However, infectious agents are important in the pathogenesis of intussusception. Primary nonenteric adenovirus infection contributes to childhood intussusception through the development of lymphoid hyperplasia in the gut.[20,21] Other viruses involved in childhood intussusception include human herpes virus-6, human herpes virus-7, and Epstein—Barr virus.[22] The epidemiology of childhood infectious agents varies between geographical areas.[7,23] Sensitivity to food antigens is associated with lymphoid nodular hyperplasia in infants, and it is interesting to note that the peak age of intussusception coincides with the usual time of weaning in many countries.[24] Whether such variations are responsible for the particular age distribution of intussusception in Taiwan needs further investigation.

In our study, the number of male patients was slightly more than that of female patients. A predominance of intussusception among male patients has also been noted in other studies, with male-to-female ratios ranging from 1.3 to 2.0.[14,16,25,26]

Table 3 Medical expenses, hospitalization stay, and coexisting neoplasms and malignancies among different age groups.

Age (y)	Inpatient service number	Average expense per inpatient service (New Taiwan Dollars)	Mean hospitalization stay (day)	Number of coexisting neoplasms (%)	Number of coexisting malignancies (%)
<1	1613	29,864	4.1	8 (0.5)	1 (0.1)
1—2	2073	16,877	3.1	7 (0.3)	0 (0)
2—3	1577	16,323	3.1	7 (0.4)	3 (0.2)
3—10	1417	18,570	3.5	25 (1.8)	11 (0.8)
10—20	100	56,252	8.6	28 (28.0)	9 (9.0)
20—60	620	72,139	10.9	22 (36.9)	103 (16.6)
60—80	439	97,103	13.7	204 (46.5)	145 (33.0)
≥80	167	114,548	15.4	67 (40.1)	50 (29.9)

Significant differences existed between pediatric and adult patients with intussusception. The incidence of intussusception was much lower in the adult patients than in the pediatric patients. Conversely, the rates of coexisting neoplasms and malignancies were much higher in the adult patients. Two review articles stated that adult intussusception is a rare condition, representing only 5% of all cases of intussusception.[11,27] However, the data used in those articles were derived from the era prior to computed tomography and ultrasonography were widely available. Adult intussusception may not be as rare as previously thought, and we found that in 15.8% of intussusception cases were aged 20 years or older. The diagnosis of intussusception in adults may be challenging due to non-specific and varying clinical presentations. Many of the adult patients with intussusceptions were brought to operating room with the preoperative diagnosis of bowel obstruction, and intussusception was discovered by the surgeon intraoperatively.[27] The increasing use of abdominal computed tomography and ultrasound will further improve the detection of intussusception. In this study, 1226 of the 8006 inpatient services were for adults. The coexisting ICD-9 codes were highly variable. The three most common coexisting ICD-9 codes in adult intussusception were 153 (malignant neoplasm of colon, 134 inpatient services), 211 (benign neoplasm of other parts of digestive system, 108 inpatient services), and 250 (diabetes mellitus, 90 inpatient services). Due to the limitation of the NHIRD, we could not confirm the etiologies of the adult intussusception based on the information obtained from the database only. However, it is reasonable to infer that the common etiologies of adult intussusception are colon cancer and benign neoplasm of the digestive system, and that many adult patients also have diabetes mellitus, as detected by the distribution of the coexisting ICD-9 codes.

We found that 24.3% of the adult patients with intussusception had coexisting ICD-9 codes of malignancy. This is similar to previous case series,[27–29] in which 20–50% cases of intussusception in adults had a malignant etiology. In the present study, the most common coexisting malignancy was colon cancer, followed by secondary malignant neoplasms of the respiratory and digestive systems, and malignant neoplasms of the small intestine including the duodenum. Colon cancer and metastatic cancer were also reported to be the most common malignancies in previous case series.[27,30] As expected, the average medical expenses and duration of hospitalization were much higher in case of adult patients due to the higher percentage of coexisting neoplasms and malignancies.

In conclusion, intussusception in children is quite different from that in adults in Taiwan. The number of male patients was slightly more than that of female patients, and the peak age of incidence was 1–2 years, which is later than that in other countries. The incidence of adult intussusception was substantially lower than that of pediatric intussusception; however, adult patients had substantially higher rates of coexisting neoplasms and malignancies and average medical expenses than pediatric patients. Adult patients with intussusception should be evaluated for neoplasms, especially for colon cancer and metastatic lesions.

Acknowledgments

References

1. Parashar UD, Holman RC, Cummings KC, Staggs NW, Curns AT, Zimmerman CM, et al. Trends in intussusception-associated hospitalizations and deaths among US infants. *Pediatrics* 2000;**106**:1413–21.
2. Bines JE, Kohl KS, Forster J, Zanardi LR, Davis RL, Hansen J, et al. Acute intussusception in infants and children as an adverse event following immunization: case definition and guidelines of data collection, analysis, and presentation. *Vaccine* 2004;**22**:569–74.
3. Bruce J, Huh YS, Cooney DR, Karp MP, Allen JE, Jewett TC Jr. Intussusception: evolution of current management. *J Pediatr Gastroenterol Nutr* 1987;**6**:663–74.
4. Meier DE, Coln CD, Rescorla FJ, OlaOlorun A, Tarpley JL. Intussusception in children: international perspective. *World J Surg* 1996;**20**:1035–9.
5. van Heek NT, Aronson DC, Halimun EM, Soewarno R, Molenaar JC, Vos A. Intussusception in a tropical country: comparison among patient populations in Jakarta, Jogyakarta, and Amsterdam. *J Pediatr Gastroenterol Nutr* 1999;**29**:402–5.
6. Gudeta B. Intussusception in children: a ten year review. *East Afr Med J* 1993;**70**:730–1.
7. Murphy TV, Gargiullo PM, Massoudi MS, Nelson DB, Jumaan AO, Okoro CA, et al. Intussusception among infants given an oral rotavirus vaccine. *N Engl J Med* 2001;**344**:564–72.
8. Kramarz P, France EK, Destefano F, Black SB, Shinefield H, Ward JI, et al. Population-based study of rotavirus vaccination and intussusception. *Pediatr Infect Dis J* 2001;**20**:410–6.
9. Patel MM, Lopez-Collada VR, Bulhoes MM, De Oliveira LH, Bautista Márquez A, Flannery B, et al. Intussusception risk and health benefits of rotavirus vaccination in Mexico and Brazil. *N Engl J Med* 2011;**364**:2283–92.
10. Buttery JP, Danchin MH, Lee KJ, Carlin JB, McIntyre PB, Elliott EJ, et al. Intussusception following rotavirus vaccine administration: post-marketing surveillance in the National Immunization Program in Australia. *Vaccine* 2011;**29**:3061–6.
11. Marinis A, Yiallourou A, Samanides L, Dafnios N, Anastasopoulos G, Vassiliou I, et al. Intussusception of the bowel in adults: a review. *World J Gastroenterol* 2009;**15**:407–11.
12. Ho WL, Yang TW, Chi WC, Chang HJ, Huang LM, Chang MH. Intussusception in Taiwanese children: analysis of incidence, length of hospitalization and hospital costs in different age groups. *J Formos Med Assoc* 2005;**104**:398–401.
13. Chen SC, Wang JD, Hsu HY, Leong MM, Tok TS, Chin YY. Epidemiology of childhood intussusception and determinants of recurrence and operation: analysis of national health insurance data between 1998 and 2007 in Taiwan. *Pediatr Neonatol* 2010;**51**:285–91.
14. Boudville IC, Phua KB, Quak SH, Lee BW, Han HH, Verstraeten T, et al. The epidemiology of paediatric intussusception in Singapore: 1997 to 2004. *Ann Acad Med Singapore* 2006;**35**:674–9.

15. Chen YE, Beasley S, Grimwood K, New Zealand Rotavirus Study Group. Intussusception and rotavirus associated hospitalisation in New Zealand. *Arch Dis Child* 2005;**90**:1077—81.
16. Tate JE, Simonsen L, Viboud C, Steiner C, Patel MM, Curns AT, et al. Trends in intussusception hospitalizations among US infants, 1993—2004: implications for monitoring the safety of the new rotavirus vaccination program. *Pediatrics* 2008;**121**:e1125—32.
17. Huppertz HI, Soriano-Gabarro M, Grimprel E, Franco E, Mezner Z, Desselberger U, et al. Intussusception among young children in Europe. *Pediatr Infect Dis J* 2006;**25**:S22—9.
18. Buettcher M, Baer G, Bonhoeffer J, Schaad UB, Heininger U. Three-year surveillance of intussusception in children in Switzerland. *Pediatrics* 2007;**120**:473—80.
19. Nelson EA, Tam JS, Glass RI, Parashar UD, Fok TF. Incidence of rotavirus diarrhea and intussusception in Hong Kong using standardized hospital discharge data. *Pediatr Infect Dis J* 2002;**21**:701—3.
20. Montgomery EA, Popek EJ. Intussusception, adenovirus, and children: a brief reaffirmation. *Hum Pathol* 1994;**25**:169—74.
21. Bhisitkul DM, Todd KM, Listernick R. Adenovirus infection and childhood intussusception. *Am J Dis Child* 1992;**146**:1331—3.
22. Hsu HY, Kao CL, Huang LM, Ni YH, Lai HS, Lin FY, et al. Viral etiology of intussusception in Taiwanese childhood. *Pediatr Infect Dis J* 1998;**17**:893—8.
23. Tian P, Ball JM, Zeng CQ, Estes MK. The rotavirus nonstructural glycoprotein NSP4 possesses membrane destabilization activity. *J Virol* 1996;**70**:6973—81.
24. Laidin AZ, Goon HK. Intussusception among infants and children in Malaysia. *Med J Malaysia* 1982;**37**:150—6.
25. Archibong AE, Usoro IN, Ikpi E, Inyang A. Paediatric intussusception in Calabar, Nigeria. *East Afr Med J* 2001;**78**:19—21.
26. Blanch AJ, Perel SB, Acworth JP. Paediatric intussusception: epidemiology and outcome. *Emerg Med Australas* 2007;**19**:45—50.
27. Azar T, Berger DL. Adult intussusception. *Ann Surg* 1997;**226**:134—8.
28. Smith IS, Gillespie G. Adult intussusception in Glasgow. *Br J Surg* 1968;**55**:925—8.
29. Harlaftis N, Skandalakis JE, Droulias C, Gray SW, Akin JT Jr. The pattern of intussusception in adults. *J Med Assoc Ga* 1977;**66**:534—9.
30. Nagorney DM, Sarr MG, McIlrath DC. Surgical management of intussusception in the adult. *Ann Surg* 1981;**193**:230—6.