Volume 201

January 2020

Download full issue

Previous vol/issue

Next vol/issue

Receive an update when the latest issues in this journal are published

Sign in to set up alerts

Download PDF Article preview

Research Articles

Research article • Full text access

Molecular eco-epidemiology on the sympatric Chagas disease vectors *Triatoma brasiliensis* and *Triatoma petrocchiae*: Ecotopes, genetic variation, natural infection prevalence by trypanosomatids and parasite genotyping

Tarcianne M. Lima-Oliveira, Fernanda von Hertwig M. Fontes, Maurício Lilioso, Dayane Pires-Silva, ... Carlos Eduardo Almeida

Article 105188

Download PDF Article preview

Research article • Full text access

Towards the optimization of botanical insecticides research: *Aedes aegypti* larvicidal natural products in French Guiana

Michaël Falkowski, Arnaud Jahn-Oyac, Guillaume Odonne, Claudiane Flora, ... Emeline Houël

Article 105179

Download PDF Article preview

Research article • Full text access

Development of a Multilocus sequence typing (MLST) scheme for Pan-*Leishmania*

Juan Jose Lauthier, Paula Ruybal, Paola Andrea Barroso, Yoshihisa Hashiguchi, ... Masataka Korenaga

Article 105189

Download PDF Article preview

Research article • Full text access

Trans-stadial fate of the gut bacterial microbiota in *Anopheles albimanus*

Yadira Galeano-Castañeda, Priscila Bascuñán, David Serre, Margarita M. Correa

Article 105204

Download PDF Article preview

Research article • Full text access

Serological tests reveal significant cross-reactive human antibody responses to Zika and Dengue viruses in the Mexican population

Mussaret Bano Zaidi, Leticia Cedillo-Barron, María Elena González y Almeida, Julio Garcia-Cordero, ... Freddy Perez

Article 105201

Download PDF Article preview

Research article • Full text access

Epidemiological survey of fasciolosis in yaks and sheep living on the Qinghai-Tibet plateau, China

Xing Gao, Lihong Zhang, Xiaole Tong, Hui Zhang, ... Jiakui Li

Article 105212

Download PDF Article preview

Research article • Full text access

Do albendazole-loaded lipid nanocapsules enhance the bioavailability of albendazole in the brain of healthy mice?

Julia Fabbri, Juan Pablo Espinosa, Patricia Eugenia Pensel, Sandra Karina Medici, ... María Celina Elissondo

Article 105215

Download PDF Article preview

Research article • Full text access

Combination of quercetin and ivermectin: *In vitro* and *in vivo* effects against *Haemonchus contortus*

Dyego Gonçalves Lino Borges, Marcelo Augusto de Araújo, Carlos Alexandre Carollo, Aline Regina Hellmann Carollo, ... Fernando de Almeida Borges

Article 105213

Download PDF Article preview

Research article • Full text access

DNA barcoding and fauna of phlebotomine sand flies (Diptera: Psychodidae: Phlebotominae) from Los Tuxtlas, Veracruz, Mexico

Yokomi N Lozano-Sardaneta, Luís E. Paternina, Sokani Sánchez-Montes, Alejandro Quintero, ... Ingeborg Becker

Article 105220

Download PDF Article preview

Research article • Full text access

In vitro activity of usnic acid potassium salt against different developmental stages of *Schistosoma mansoni*: An ultrastructural study

Hallysson D.A. Araújo, Victor H.B. Santos, Fábio A. Brayner, Luiz C. Alves, ... Vera L.M. Lima

Article 105159

Download PDF Article preview

Research article • Full text access

Real-time PCR to differentiate among *Leishmania* (*Viannia*) subgenus, *Leishmania* (*Leishmania*) *infantum* and *Leishmania* (*Leishmania*) *amazonensis*: Application on Brazilian clinical samples

Aurora Diotallevi, Gloria Buffi, Marcello Ceccarelli, Herintha Coeto Neitzke-Abreu, ... Luca Galluzzi

Article 105178

Download PDF Article preview

Research article • Full text access

Seroprevalence of *Toxoplasma gondii* in horses: A global systematic review and meta-analysis

Xi Li, Hong-Bo Ni, Wei-Xin Ren, Jing Jiang, ... Xiao-Xuan Zhang

Article 105222

Download PDF Article preview

Short Communications

Short communication • Full text access

Gender beyond male and female: Occurrence of a gynandromorph in the Japanese encephalitis vector *Culex sitiens* (Diptera: Culicidae)

Van Lun Low, Meng Li Wong, Jonathan Wee Kent Liew, Sandthya Pramasivan, ... Indra Vythilingam

Article 105207

Download PDF Article preview

Short communication • Full text access

A hyperendemic focus of porcine cystic echinococcosis in the Banke District of Nepal

Meritxell Donadeu, Charles G. Gauci, Ishab Poudel, Keshav Sah, ... Marshall W. Lightowlers

Article 105203

Download PDF Article preview

Short communication • Full text access

Vancomycin and florfenicol resistant *Enterococcus faecalis* and *Enterococcus faecium* isolated from human urine in an Egyptian urban-rural community

Kamelia Osman, Tara Rava Zolnikov, Jihan Badr, Heba Naim, ... Ayman Elbehiry

Article 105209

Download PDF Article preview

Short communication • Full text access

Functional insight into the glycosomal peroxiredoxin of *Leishmania*

Helena Castro, Maria Inês Rocha, Ricardo Silva, Filipe Oliveira, ... Ana Maria Tomás

Article 105217

Download PDF   Article preview

Short communication • Full text access

Molecular cytotaxonomy of the *Triatoma brasiliensis* species subcomplex (Hemiptera, Triatominae)

Kaio Cesar Chaboli Alevi, Isadora de Freitas Bittinelli, Luiza Maria Grzyb Delgado, Fernanda Fernandez Madeira, ... Maria Tercília Vilela Azeredo-Oliveira

Article 105225

Download PDF   Article preview

Letter to the Editor

Correspondence • Full text access

Is Amazonian Toxoplasmosis a real risk for Brazil?

Claudio Bruno Silva de Oliveira

Article 105216

Download PDF

Status and Perspective of Helminthisasis in China

Research article • Full text access

Intestinal microbiome profiles in *Oncomelania hupensis* in mainland China

Yuwan Hao, Wei Guan, Haonan Wu, Lanhua Li, ... Shizhu Li

Article 105202

Download PDF   Article preview

Research article • Full text access

Sanguinarine has anthelmintic activity against the enteral and parenteral phases of *trichinella* infection in experimentally infected mice

Haibin Huang, Jiayun Yao, Ke Liu, Wentao Yang, ... Guilian Yang

Article 105226

Download PDF   Article preview

Review article • Full text access

From parasitic disease control to global health: New orientation of the National Institute

of Parasitic Diseases, China CDC
Jin Chen, Wei Ding, Zhen Li, Dan-Dan Zhou, ... Xiao-Nong Zhou
Article 105219

Download PDF Article preview

New advances in the treatment of Chagas Disease

Research article • *Open access*
The effect of benznidazole dose among the efficacy outcome in the murine animal model. A quantitative integration of the literature
Israel Molina, Luisa Perin, Augusto Sao Aviles, Paula Melo de Abreu Vieira, ... Claudia M. Carneiro
Article 105218

Download PDF Article preview

Special issue: NTD Asia 2019

Review article • Full text access
Leptospirosis: Increasing importance in developing countries
Zoey May Pheng Soo, Naveed Ahmed Khan, Ruqaiyyah Siddiqui
Article 105183

Download PDF Article preview

Research article • Full text access
Preliminary evaluation of the diagnostic potential of *Schistosoma japonicum* extracellular vesicle proteins for *Schistosomiasis japonica*
Yongjun Chen, Bikash Ranjan Giri, Xue Li, Xiaobing He, ... Guofeng Cheng
Article 105184

Download PDF Article preview

Review article • Full text access
Foodborne intestinal flukes: A brief review of epidemiology and geographical distribution
Jong-Yil Chai, Bong-Kwang Jung
Article 105210

Download PDF Article preview

Research article • Full text access
Neurocysticercosis cases identified at Sanglah Hospital, Bali, Indonesia from 2014 to 2018
Ni Made Susilawathi, AA Ayu Suryapraba, Andreas Soejitno, Made Widhi Asih, ... AA Raka Sudewi
Article 105208

Research article • Full text access

Genotyping of *Enterocytozoon bieneusi* among captive long-tailed macaques (*Macaca fascicularis*) in Hainan Province: High genetic diversity and zoonotic potential

Wei Zhao, Huanhuan Zhou, Hairong Jin, Lijie Sun, ... Gang Lu

Article 105211

Research article • Full text access

The combination of Cytokines and albendazole therapy for prophylaxis and treatment of experimental/hydatid cyst

M. Rahdar, A. Rafiei, R. Valipour- Nouroozi

Article 105206

Research article • Full text access

Behavior-related risk factors for opisthorchiasis-associated cholangiocarcinoma among rural people living along the mekong river in five greater mekong subregion countries

Nopparat Songserm, Pattaraporn Charoenbut, Onanong Bureelerd, Kanjanar Pintakham, ... Banchop Sripa

Article 105221

ISSN: 0001-706X

ACTA TROPICA

Processed at Thomson Digital, Gangtok (India)

Acta Tropica 201 (2020) 105208

Contents lists available at ScienceDirect

Acta Tropica

journal homepage: www.elsevier.com/locate/actatropica

Neurocysticercosis cases identified at Sanglah Hospital, Bali, Indonesia from 2014 to 2018

Ni Made Susilawathi[a,1,*], AA Ayu Suryapraba[a,1], Andreas Soejitno[a,1], Made Widhi Asih[b], Kadek Swastika[c], Toni Wandra[d,1], Christine M. Budke[e,1], Akira Ito[f,1,*], AA Raka Sudewi[a]

[a] Department of Neurology, Faculty of Medicine, Udayana University, Bali, Indonesia
[b] Department of Radiology, Faculty of Medicine, Udayana University, Bali, Indonesia
[c] Department of Parasitology, Faculty of Medicine, Udayana University, Bali, Indonesia
[d] Directorate of Postgraduate, Sari Mutiara Indonesia University, Medan, Indonesia
[e] Department of Veterinary Integrative Biosciences, College of Veterinary Medicine & Biomedical Sciences, Texas A & M University, College Station, TX, USA
[f] Department of Parasitology and Laboratory of NTDs, Asahikawa Medical University, Asahikawa, Japan

ARTICLE INFO

Keywords:
Neurocysticercosis
Taenia solium
Sanglah Hospital
Bali
East Nusa Tenggara
Timor-Leste

ABSTRACT

Neurocysticercosis (NCC) was first reported in the province of Bali, Indonesia in 1975. Since this time, sporadic cases have been reported annually. This study reports information on 29 NCC cases (20 males and 9 females) admitted to a referral hospital in Denpasar, Bali from 2014 until 2018. Twenty-four cases were from Bali, 2 were from the province of East Nusa Tenggara, and 3 were from the Democratic Republic of Timor-Leste. Mean patient age was 37.2 years and 69.0% (20/29) were male. Epileptic seizures were the most common clinical manifestation (65.5%, 19/29). Serology (ELISA) was used in 14 cases (48.2%, 14/29), but only 6 cases, including one case with an inactive calcified lesion, were positive (42.9%, 6/14). Two cases underwent surgical resection after their lesions were initially misdiagnosed as brain tumors. These hospital-based findings are discussed along with the present status of NCC in Bali.

1. Introduction

Neurocysticercosis (NCC) is a parasitic zoonosis often found in areas where meat inspection and sanitation practices are insufficient (Schantz et al., 1998). One endemic area is the Asia-Pacific region (Aung and Spelman, 2016; Ito and Budke, 2014; Ito et al., 2003, 2014, 2019; Rajshekhar et al., 2003; Singh et al., 2002; Sutisna et al., 2019; Wandra et al., 2015). As summarized by Ito et al. (2004, 2019) and Sutisna et al. (2019), NCC has been identified in Bali since 1928 (Le Coultre, 1928; Lie et al., 1955; Ngoerah, 1975) and in Papua, Indonesia since 1973 (Desowitz, 1981; Gajdusek 1978; Tumada and Margono, 1973; reviewed by Margono et al. (2001, 2006), Simanjuntak et al. (1997), Suroso et al. (2006) and Wandra et al. (2006).

Human taeniasis, caused by *T. solium,* is transmitted through eating uncooked or undercooked pork harboring *T. solium* cysticerci. Since the majority of the Indonesian population (87.18%) (Sutisna et al., 2019; Wandra et al., 2013) is Muslim, religious restrictions on the keeping of pigs and preparation and consumption of pork have limited the impact of *T. solium* in most of Indonesia. Exceptions include Papua where most of the local population is Christian and Bali where most of the local population is Hindu. Although *T. solium* is suspected of circulating in additional provinces, there has been only a single reported case of NCC in a 46-year-old man from Sumba in the province of East Nusa Tenggara (Sudewi et al., 2013) and unpublished serological screening data from Timor Leste (Reeve, 2010).

In Bali, a case of disseminated cysticercosis was confirmed in a local woman in 2001 (Margono et al., 2002). Additional sporadic NCC cases have been reported by Sudewi and Nuartha (1998a, 1988b, 1998c), Sudewi et al. (2008), Sutisna (1993), Swastika et al. (2012) and Wandra et al. (2011, 2016). More recent community-based studies (Ito et al., 2019; Sutisna et al., 2019) have confirmed *T. solium* transmission in focal areas along the northeastern slope of Mt. Agung in the Kubu and Abang subdistricts of Karangasem (Swastika et al., 2012, 2016, 2017). In these areas, the local people still consume uncooked pork and transmission of *T. solium* is actively maintained between tapeworm carriers and free-roaming pigs. This is in contrast to most areas in Bali, where consumption of undercooked pork is uncommon and pigs are

* Corresponding authors.
E-mail addresses: susilawathi@unud.ac.id (N.M. Susilawathi), akiraito@asahikawa-med.ac.jp (A. Ito).
[1] These authors worked equally for preparation of the MS.

https://doi.org/10.1016/j.actatropica.2019.105208
Received 30 March 2019; Received in revised form 3 October 2019; Accepted 3 October 2019
Available online 04 October 2019

reared indoors with no access to human feces (Sutisna et al., 2019). Since inhabitants of Karangasem are known to go to the local capital city of Denpasar to find work during the dry season, there is the risk that a tapeworm carrier from an endemic area will infect others in a non-endemic area (Wandra et al., 2016).

This paper reports 29 NCC cases identified at a referral hospital (Sanglah Hospital, Udayana University) in Denpasar, Bali from 2014 until 2018. These hospital cases are discussed along with recent epidemiological studies conducted in Bali (Sudewi et al., 2008; Sutisna et al., 2019; Swastika et al., 2012, 2016, 2017; Wandra et al., 2006, 2011, 2013, 2015, 2016).

2. Materials and methods

Medical record reviews were conducted for patients diagnosed with NCC at Sanglah Hospital from January 2014 through November 2018. Data on demographics, clinical manifestations, neuroimaging findings, serology, and lesion pathology were collected. If any of this information was not available in the medical records, there was an attempt to collect the information during the patient's next scheduled follow-up appointment. Complete patient travel histories were not available. A diagnosis of NCC was based on criteria established by Carpio et al. (2016) and Del Brutto et al. (2017). Seizures were classified according to the 1981 International League Against Epilepsy (ILAE) seizure classification (Anonymous, 1981). Neuroimaging results (head computed tomography (CT) scan and magnetic resonance imaging (MRI)) were interpreted by board-certified neuroradiologists. Serological examination by ELISA was carried out using partially purified low molecular weight (LMW) antigens (Sako et al., 2013). Descriptive data were evaluated using proportions or means (± standard deviation).

Patients were categorized based on whether or not they came from a *T. solium*-endemic area. For this purpose, an endemic area was defined as a region where active *T. solium* transmission (i.e., completion of the human-pig-human life cycle) and one or more cases of locally acquired *T. solium* cysticercosis in humans and/or pigs had been confirmed in the last 3 years. A village was considered endemic if one or more banjar (the smallest administrative unit) was endemic. A subdistrict was considered endemic if it contained one or more endemic village and a district was considered endemic if it contained one or more endemic subdistrict.

This study was approved by the Research Ethics Committee of the Faculty of Medicine, Udayana University, Bali, Indonesia (Number 123/ UN.14.2/ KEP/2016, dated September 26, 2016).

3. Results

In total, 29 NCC cases were identified in 2014 (n = 9), 2015 (n = 6), 2016 (n = 6), 2017 (n = 5), and 2018 (n = 3) (Table 1). Of the 29 cases, 20 (69.0%) were male. Mean patient age was 37.2 ± 17.6 years (range: 13–79 years). Mean age in males and females was 36.3 ± 14.8 (range: 14–61 years) and 39.2 ± 23.6 (range: 13–79 years), respectively. The numbers of NCC cases with solitary and multiple lesions were 11 (8 males and 3 females) and 18 (12 males and 6 females), respectively. According to currently accepted NCC diagnostic criteria (Carpio et al., 2016), 15 patients (51.7%) were definitively diagnosed with parenchymal NCC, 10 patients (34.5%) were diagnosed with probable parenchymal NCC, 3 patients (10.3%) were definitively diagnosed with extra-parenchymal NCC, and one patient (3.4%) was definitively diagnosed with NCC with both parenchymal and extra-parenchymal (intraventricular) cysts. In comparison, when using the most recent version of Del Brutto et al. diagnostic criteria (Del Brutto et al., 2017), 58.6% (17/29) and 41.4% (12/29) of cases were diagnosed as definitive and probable NCC, respectively. Based on neuroimaging classification (Zhao et al., 2015), 60% (15/25) of patients with definitive or probable parenchymal NCC had active cyst stages. Serology (ELISA) was used in 14 cases (48.2%, 14/29), but only 6 cases

Table 1
Summarized data of 29 NCC cases confirmed at Sanglah Hospital 2014–2018 (NCC: neurocysticercosis, DCC: disseminated cysticercosis).

Year	Number of cases (sex)/Ethnicity (sex)	Diagnosed	Methods for examination	Main symptoms
2014	9 cases (5 M, 4F)/all Balinese	NCC	CT scan, MRI, Serology	Epileptic seizures, headaches
2015	6 cases (4 M, 2F)/3 Balinese (3 M)/3 from East Timor (1 M, 2F)	NCC	CT scan, MRI, Serology	Epileptic seizures, headaches
2016	6 cases (5 M, 1F)/5 Balinese (4 M, 1F) 1 M from East Nusa Tenggara	NCC	CT scan, MRI, Serology	Epileptic seizures, headaches, Brun's syndrome, stroke like syndrome
2017	5 cases (3 M, 2F)/4 Balinese (2 M, 2F) 1 M from East Nusa Tenggara	4 NCC 1 DCC	CT scan, MRI, Serology, x ray (chest)	Epileptic seizures, headaches, hemiparesis, subcutaneous nodule
2018	3 cases (3 M)/all Balinese	2 NCC 1 DCC	CT scan, MRI, Serology, x ray (chest, humerus, femur)	Epileptic seizures, headaches, hemiparesis

Table 2
Demographics, clinical manifestations, and diagnostic test results associated with 29 NCC patients treated at Sanglah Hospital, Bali during 2014–2018.

Characteristics	Number of patients (%)
Age (mean ± SD/year)	37.2 ± 17.6
Sex	
Male	20 (69.0)
Female	9 (31.0)
Region (district)	
Denpasar	10 (34.5)
Gianyar	5 (17.2)
Buleleng	5 (17.2)
Badung	3 (10.3)
Karangasem	1 (3.4)
Outside Bali	5 (17.2)
Clinical manifestations	
Seizure	19 (65.5)
General tonic clonic seizure	13 (68.4)
Simple partial seizure	2 (10.5)
Secondary generalized partial seizure	4 (21.1)
Headaches	5 (17.2)
Hemiparesis	3 (10.3)
Bruns syndrome	2 (6.9)
Tumor-like syndrome	5 (17.2)
Signs of increased intracranial pressure	3 (10.3)
Neuropshychiatric disorder	1 (3.5)
Neuroimaging modalities	
Head CT scan	16 (55.2)
Head MRI	9 (31.0)
Head CT scan and MRI	4 (13.8)
Number of lesions on neuroimaging	
Single	11(37.9)
Male	8 (72.7)
Female	3 (27.3)
Multiple	18 (62.1)
Male	12 (66.7)
Female	6 (33.3)
Neuroimaging classification according to Zhao et al.	
Intraparenchymal NCC	25 (86.2)
Vesicular (active)	5 (20.0)
Colloidal vesicular (active)	5 (20.0)
Granular nodular (active)	5 (20.0)
Nodular calcified (inactive)	10 (40.0)
Intraventricular NCC (active)	4 (13.8)
Other imaging findings for disseminated NCC (n = 2)	
Chest x-ray	1 (50.0)
Thigh x-ray (part of bone survey)	1 (50.0)
Serology (n = 14)	
Positive	6 (42.9)
Vesicular	2 (33.3)
Colloidal vesicular	0 (0)
Granular nodular	1 (16.7)
Nodular calcified	2 (33.3)
Intraventricular	1 (16.7)
Negative	8 (57.1)
Diagnosis based on Carpio's criteria	
Definitive parenchymal NCC	15 (51.7)
Probable parenchymal NCC	10 (34.5)
Definitive extraparenchymal NCC	3 (10.3)
Definitive parenchymal and extraparenchymal NCC	1 (3.4)
Diagosis based on Del Brutto's criteria	
Definitive	17 (58.6)
Probable	12 (41.4)

(42.9%, 6/14), including one case with an inactive calcified lesion, were positive.

Table 2 shows presenting symptoms, with epileptic seizures the most common clinical manifestation (65.5%, 19/29). Seizure types included general tonic-clonic seizures (68.4%, 13/19), simple partial seizures (10.5%, 2/19), and secondary generalized partial seizures (21.1%, 4/19). Two patients (6.9%) developed Bruns syndrome due to episodic obstructive hydrocephalous, with symptoms including severe headaches, vertigo, and vomiting, particularly after head movement. Two NCC cases underwent surgical resection after their lesions (coloidal vesicular cysts) were initially misdiagnosed as brain tumors (one misdiagnosed as a glioma and the other as a meningioma).

In terms of geographic origin, 24 cases (82.8%) were from Bali (Fig. 1A). Among the 24 Balinese cases, 23 were from non-endemic areas, including the city of Denpasar (10 cases), Buleleng District (5 cases), Gianyar District (5 cases), and Badung District (3 cases). One case was from the endemic district of Karangasem (Fig. 1B). The additional five cases were from outside of Bali and included 2 cases from East Nusa Tenggara Province and 3 cases from Timor-Leste (Fig. 1A).

4. Discussion

In this study, seizures were the most common clinical manifestations (65.5%, 19/29) that urged patients to seek professional medical care, followed by severe chronic headaches (17.2%, 5/29). Other serious complications included hemiparesis, with 3 NCC patients presenting with hemiparesis of over a 6-month duration. Symptoms in one of these patients was initially believed to be due to a stroke. However, it was determined that this patient had an NCC lesion pressing on the basal ganglia, thus mimicking stroke. Two Bruns syndrome cases were treated with ventriculo-peritoneal shunt placement (Torres-Corzo et al., 2006). Intraventricular NCC was commonly associated with hydrocephalus due to obstruction of cerebrospinal fluid drainage.

Both Carpio's diagnostic criteria (Carpio et al., 2016) and the newer classification scheme by Del Brutto et al. (2017) were used for the classification of NCC lesions in this study. Although the latter criteria have only been partially validated, the resulting categorization, using these two schemes, did not differ substantially (55% and 58% of NCC cases considered definitive by Carpio et al. (2016) and Del Brutto et al. (2017), respectively). A number of cases were considered probable versus definitive due to the absence of evidence indicating an active disease stage (i.e., the presence of an active parenchymal cyst with or without an invaginated scolex) or the absence of multiple lesion forms in various stages of evolution seen on neuroimaging. In addition, only two patients with parenchymal cysts had their NCC diagnosis confirmed by pathology.

Contrary to what was stated by Del Brutto et al. (2017), we found that the majority (93.1%, 27/29) of active NCC cyst stages were found in cortical areas, while only a few (6.9%, 2/29) were located in the cortical-subcortical junction or basal ganglia. No active cysts were located in the brainstem, but the two cases that developed Bruns syndrome had lesions in the cerebellum, causing non-communicating hydrocephalus. We also found two NCC cases with multiple subcutaneous nodules. One patient had multiple nodules on chest x-ray evaluation (Fig. 2A), while the other had multiple nodules in the thigh (Fig. 2B).

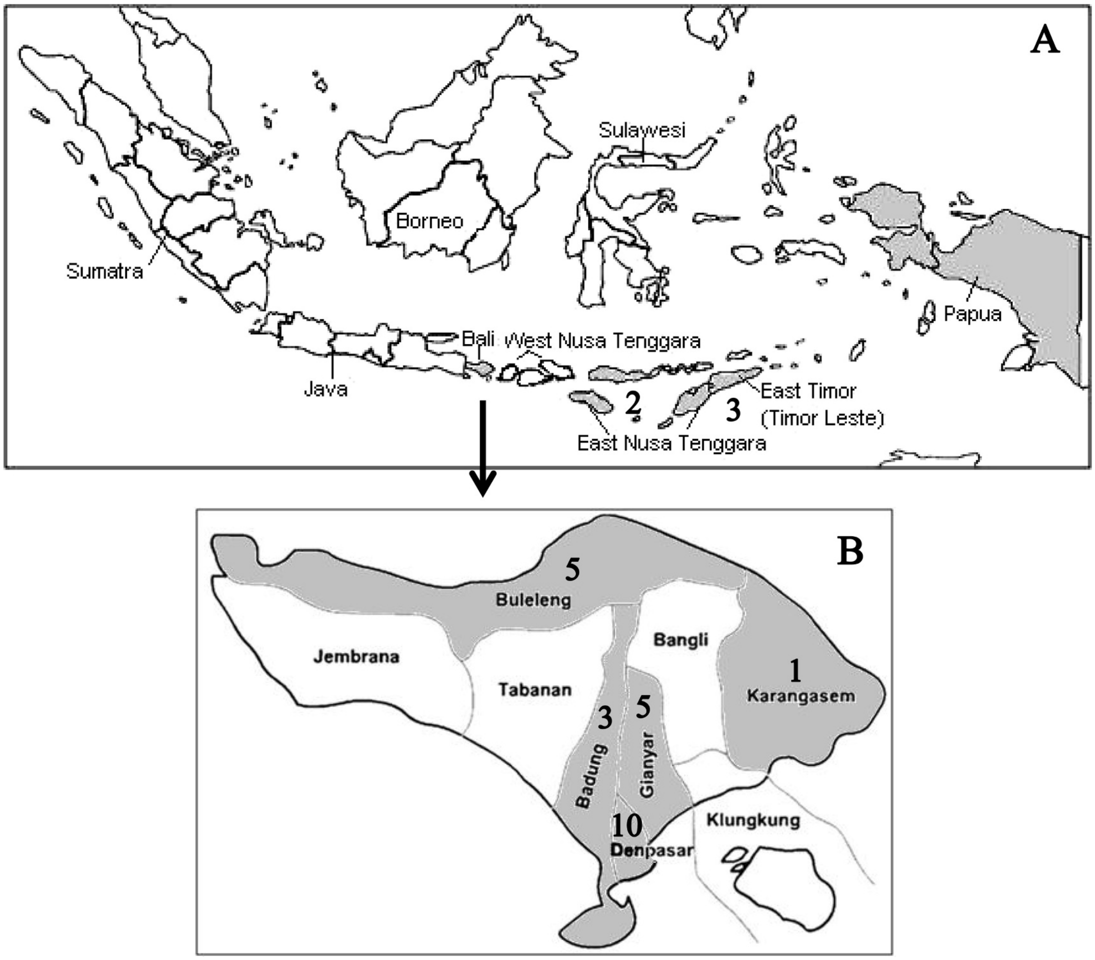

Fig. 1. Map of Indonesia, including East Timor (A) and Bali (B), showing the five districts where the NCC cases admitted to Sanglah Hospital in Denpasar originated. Fig. 1-B was derived from Wikimedia Commons (available at: https://commons.wikimedia.org/wiki/File:Indonesia_provinces_blank.png) licensed under Creative Commons Attribution-Share Alike 3.0.

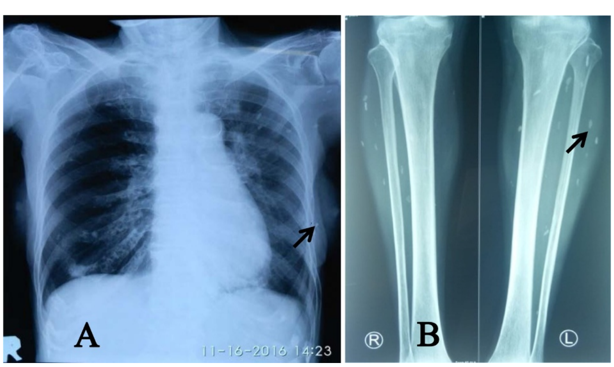

Fig. 2. Subcutaneous nodules identified on (A) chest x-ray (79-year-old female), and (B) in the left and right anterior thigh (61-year-old male).

Interestingly, both of these patients were categorized as having definitive NCC according to both the Carpio and Del Brutto classification schemes. Subcutaneous nodules may not be easily apparent on clinical examination, thus necessitating further screening (Sacchidanand et al., 2012). Unfortunately, one patient with nodules in the chest did not yield a positive serology result, while a subject with nodules in the thigh did not undergo serological evaluation due to the patient's refusal to consent to the collection of a blood sample.

CT scan was the most often utilized diagnostic imaging method in the current case series (55.2%, 16/29), although a number of cases (31.0%, 9/29) received head MRI, most commonly to investigate seizure activity suspected of being due to a structural lesion (Cendes et al., 2016; Palmeri et al., 2011). A CT scan followed by an MRI was occasionally performed for more challenging cases (13.8%, 4/29) (Fig. 3). Two patients with the colloidal vesicular stage were initially diagnosed as having brain tumors. A similar case was reported in Japan (Ito et al., 1999; Yanagida et al., 2010). In the Japanese case, the original serological evaluation did not indicate *T. solium* infection. However, serological evaluation using a different test showed a clear antibody response before surgery, with no detectable antibody response within one year after surgery (Ito et al., 1999). Serological detection of cysticercosis-specific antibody responses can be a valuable diagnostic tool (Del Brutto et al., 2017; Ito, 2002; Ito et al., 1998; Sato et al., 2006).

In the current case series, the majority of cases were male (69.0%, 20/29). This may be due to differences in the rate of autoinfection (Ito et al., 2019; Schantz and Kramer, 1995; Schantz et al., 1998) or differences in the amount of undercooked pork consumed by males and females. For example, *lawar* (a dish frequently made with uncooked pork) may be more often consumed by males during certain ceremonial events such as *mebat* (Margono, 1989; Sutisna et al., 2019). Based on a recent epidemiological survey in Bali, the *T. solium* life cycle has only been confirmed in the Kubu and Abang sub-districts of Karangasem (Ito et al., 2019; Sudewi et al., 2008; Sutisna et al., 2019; Swastika et al., 2012, 2016, 2017; Wandra et al., 2015, 2016). Due to the need to support their families during the dry season, members of this largely agricultural population often go to larger towns or cities to find work. As a result, it is suspected that tapeworm carriers from Karangasem may

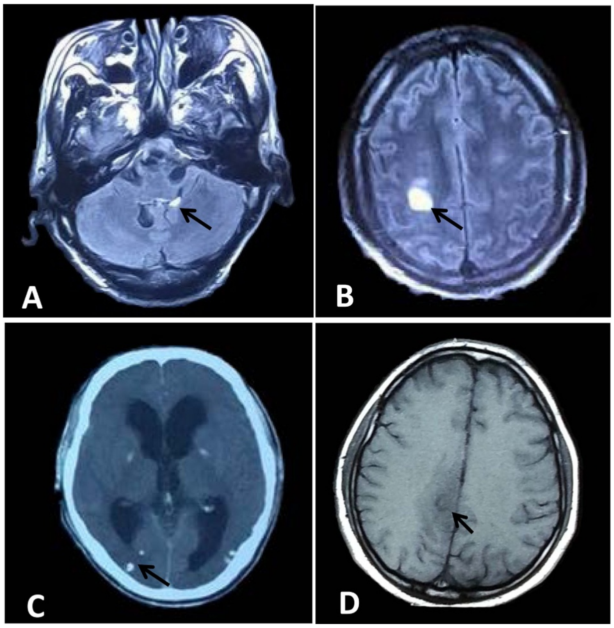

Fig. 3. Neuroimaging of a 38-year-old male demonstrating multiple pathological stages. (A) Axial T2WI MRI of infratentorial vesicular stage lesions. The cyst signaled on A appears to be colloidal. Two probable vesicular cysts also appear in this image: in the fourth ventricle lateral recess (right) and in the left peribulbar cistern. (B) Flair sequence MRI of a granular nodular stage lesion on the right centrum semiovale. The cyst appears to be vesicular-colloidal. (C) CT scan of calcified nodular stage lesions on both hemispheres. (D) T1WI MRI of a lesion with characteristics of both the colloidal and nodular/granular stage on the right centrum semiovale.

contaminate urban or semi-urban environments in other districts (Wandra et al., 2016). In support of this hypothesis, symptomatic NCC cases have been confirmed in nearby cities and towns, including Denpasar, Gianyar, Badung, and Buleleng.

Not all NCC patients in rural areas have access to medical treatment. In contrast, NCC cases in urban or semi-urban areas have greater access to hospital care. Prior to the current study, only a single ocular cysticercosis case was reported from Indera Hospital in Denpasar (Swastika et al., 2012). In addition, there was an NCC case report of a migrant from Karangasem confirmed in Gianyar in 2007. This individual initially presented with taeniasis, which was believed to have been due to *T. saginata* infection based on morphological identification of discharged gravid proglottids. The patient was subsequently treated with praziquantel. He was later diagnosed with NCC after having a seizure (Wandra et al., 2016).

NCC is associated with poverty and poor sanitation (WHO, 2014). For the last several decades, *T. solium* control programs have been implemented in Bali at the district level. These programs focus on improving biosecurity measures for pigs, including preventing access to human feces, as well as improving personal hygiene and environmental sanitation (Wandra et al., 2015; Ministry of Health Republic of Indonesia, 2014). These initiatives, along with an improved local economy, are likely responsible for a decrease in *T. solium* transmission in most areas of Bali (Ito et al., 2019; Sutisna et al., 2019), resulting in fewer cases of NCC. While there has been steady progress made in decreasing *T. solium* transmission, recent attempts to eradicate NCC have been made even more difficult by repeated eruptions of Mt. Agung since 2017. Because of the eruptions, people from the affected districts of Karangasem and Singaraja have needed to seek shelter in refugee centers or travel to other regions, including Denpasar to find housing and work. The eruptions also exacerbate existing difficulties with access to clean water in this region. It is a concern that migration of *T. solium* carriers may result in an increase in NCC cases in non-endemic areas, such as Denpasar.

Additional studies are needed to evaluate the extent of ongoing *T. solium* transmission in the district of Karangasem. More than 60% of NCC cases (62.1%, 18/29), in the current study, were confirmed to have multiple lesions. As NCC cases can be asymptomatic for many years (Ito et al., 1999; Yanagida et al., 2010), it is common for NCC cases to not have taeniasis at the time of diagnosis even if they were previously infected (Garcia et al., 2003; Ito et al., 2019; Lightowlers, 2010; Sarti et al., 1988, 1992; Schantz et al., 1998). *T. solium* tapeworm carriers with disseminated cysticercosis are at high risk for NCC along with their close family members. Previous studies have indicated that from 5% to 40% of disseminated cases have concurrent taeniasis (Garcia et al., 2003; Schantz and Kramer, 1995; Schantz et al., 1998).

Microscopy for detection of *Taenia* eggs (Swastika et al., 2017) followed by real time molecular differentiation of the infecting species (Nkouawa et al., 2010) has been recommended for screening of *T. solium* taeniasis carriers. At that same time, serologic screening for cysticercosis and NCC is also recommended (Swastika et al., 2016). An epidemiological survey conducted in Bali from 2011 until 2017 confirmed a total of 20 *T. solium* tapeworm carriers (19 from Karangasem) (Swastika et al., 2017). All carriers were seronegative for cysticercosis (Swastika et al., 2016). Additional studies are needed to determine if this population is somehow more resistant to acquiring cysticercosis.

The current study revealed 2 NCC cases from East Nusa Tenggara and 3 cases from Timor-Leste (Fig. 1). This is the second published record of NCC from East Nusa Tenggara (Sudewi et al., 2013) and the first record from Timor-Leste (Braae et al., 2018; Ito et al., 2004; Reeve, 2010). East Nusa Tenggara is considered a non-endemic area for *T. solium* cysticercosis (Sutisna et al., 2019) and there is a single study where a serologic survey was conducted in Timor-Leste (Reeve, 2010). Serum samples from Timor-Leste (345 samples from thee different areas), Papua New Guinea (191 samples from 4 different areas), and Papua (51 samples from Timika) were tested with both ELISA and immunoblot using purified antigens (Ito et al., 1998) and recombinant antigens (Sako et al., 2000). Overall seropositivity in Timor-Leste was 1.7% (6/345), with 2.1% (5/191) of samples positive from Papua New Guinea, and 2.0% (12/587) of samples positive from Timika, Papua. Additional studies are needed to better elaborate the situation in these areas (Ito et al., 2003, 2004; Wandra et al., 2003).

5. Conclusion and perspectives

Field surveys should be conducted in East Nusa Tenggara and Timor-Leste to determine if there is active *T. solium* transmission. Elimination of taeniasis and cysticercosis in Bali is an important goal, especially since the island has more than 5 million visitors annually. However, such an effort will require collaboration between multiple agencies and sectors, including the Indonesia Ministry of Health, provincial and district level health agencies, community health centers, the livestock sector, and tourism associations.

Financial support

This study was supported by The Research and Development of the Faculty of Medicine, Udayana University of Bali in 2016.

Declaration of Competing Interest

Authors had no conflict of interest to declare.

Acknowledgments

We sincerely thank David Blair for providing the authors with access to the Ph.D. dissertation by D.M. Reeve (2010).

References

Anonymous, 1981. Proposal for revised clinical and electroencephalographic classification of epileptic seizures. From the commission on classification and terminology of the international league against epilepsy. Epilepsia 22, 489–501.

Aung, A.K., Spelman, D.W., 2016. *Taenia solium* taeniasis and cysticercosis in Southeast Asia. Am. J. Trop. Med. Hyg. 94, 947–954.

Braae, E.C., Hung, N.M., Satrija, F., Khieu, V., Zhou, X.N., Willingham, A.L., 2018. Porcine cysticercosis (*Taenia solium* and *Taenia asiatica*): mapping occurrence and areas potentially at risk in East and Southeast Asia. Parasit. Vectors 11, 613.

Carpio, A., Fleury, A., Romo, M.L., Abraham, R., Fandino, J., Duran, J.C., 2016. New diagnostic criteria for neurocysticercosis: reliability and validity. Ann. Neurol. 80, 434–442.

Cendes, F., Theodore, W.H., Brinkmann, B.H., Sulc, V., Cascino, G.D., 2016. Neuroimaging of epilepsy. Handb. Clin. Neurol. 136, 985–1014.

Del Brutto, O.H., Nash, T.E., White Jr., A.C., Rajshekhar, V., Wilkins, P.P., Singh, G., Vasquez, C.M., Salgado, P., Gilman, R.H., Garcia, H.H., 2017. Revised diagnostic criteria for neurocysticercosis. J. Neurol. Sci. 372, 202–210.

Desowitz, R.S., 1981. New Guinea Tapeworms and Jewish grandmothers: Tales of Parasites and People. W.W. Norton & Company, New York.

Gajdusek, D.C., 1978. Introduction of Taenia solium into West New Guinea with a note on an epidemic of burns from cysticercosis epilepsy in the Ekari people of the Wissel Lakes area. Papua New Guinea Med. J. 21, 329–342.

García, H.H., Gilman, R.H., Gonzalez, A.E., Verastegui, M., Rodriguez, S., Gavidia, C., Tsang, V.C., Falcon, N., Lescano, A.G., Moulton, L.H., Bernal, T., Tovar, M., Cysticercosis Working Group in Perú, 2003. Hyperendemic human and porcine *Taenia solium* infection in Peru. Am. J. Trop. Med. Hyg. 68, 268–275.

Ito, A., 2002. Serologic and molecular diagnosis of zoonotic larval cestode infections. Parasitol. Int. 51, 221–235.

Ito, A., Budke, C.M., 2014. Culinary delights and travel? A review of zoonotic cestodiases and metacestodiases. Travel Med. Infect. Dis. 12, 582–591.

Ito, A., Nakao, M., Wandra, T., 2003. Human taeniasis and cysticercosis in Asia. Lancet 362, 1918–1920.

Ito, A., Li, T., Wandra, T., Dekumyoy, P., Yanagida, T., Okamoto, M., Budke, C.M., 2019. Taeniasis and cysticercosis in Asia: a review with emphasis on molecular approaches and local lifestyles. Acta Trop. 198, 105075.

Ito, A., Nakao, M., Ito, Y., Yuzawa, I., Morishima, H., Kawano, N., Fujii, K., 1999. Neurocysticercosis case with a single cyst in the brain showing dramatic drop in specific antibody titers within 1 year after curative surgical resection. Parasitol. Int. 48, 95–99.

Ito, A., Plancarte, A., Ma, L., Kong, Y., Flisser, A., Cho, S.Y., Liu, Y.H., Kamhawi, S., Lightowlers, M.W., Schantz, P.M., 1998. Novel antigens for neurocysticercosis: simple method for preparation and evaluation for serodiagnosis. Am. J. Trop. Med. Hyg. 59, 291–294.

Ito, A., Wandra, T., Li, T., Dekumyoy, P., Nkouawa, A., Okamoto, M., Budke, C.M., 2014. The present situation of human taeniasis and cysticercosis in Asia. Recent Pat. Antiinfect. Drug Discov. 9, 173–185.

Ito, A., Wandra, T., Yamasaki, H., Nakao, M., Sako, Y., Nakaya, K., Margono, S.S., Suroso, T., Gauci, C., Lightowlers, M.W., 2004. Cysticercosis/taeniasis in Asia and the Pacific. Vector Borne Zoonotic Dis. 4, 95–107.

Le Coultre, A.P., 1928. Cysticerci in Beef and Pork. A Study on Hygiene After a Special Investigation of These Parasites on the Island of Bali. University of Utrecht, Netherlands, pp. 248 Thesis.

Lie, K.J., Gupito, C., Handojo, K., 1955. A case of cysticercosis in Indonesia. Doc. Med. Geogr. Trop. 7, 134–135.

Lightowlers, M.W., 2010. Eradication of *Taenia solium* cysticercosis: a role for vaccination of pigs. Int. J. Parasitol. 40, 1183–1192.

Margono, S.S., 1989. Cestodes in man in Indonesia. Bul. Penelit. Kesehat. 17, 60–66.

Margono, S.S., Ito, A., Suroso, T., 2001. The problem of taeniasis and cysticercosis in Irian Jaya, Indonesia. Med. J. Indones. 10, 110–114.

Margono, S.S., Himawan, S., Purnama, T.A., Subahar, R., Hamid, A., Ito, A., 2002. Multiple cysticercus nodules in skin and brain in a Balinese woman: a case report. Med. J. Indones. 11, 169–173.

Margono, S.S., Wandra, T., Swasono, M.F., Muri, S., Craig, P.S., Ito, A., 2006. Taeniasis/cysticercosis in Papua (Irian Jaya), Indonesia. Parasitol. Int. 55, S143–S148.

Ministry of Health Republic of Indonesia. 2014. Regulation of Minister of Health Republic of Indonesia Number 3 Year 2014 on Community-based total sanitation (in Indonesian).

Ngoerah, I., 1975. Cysticercosis of the Brain 9. Majalah Ilmiah Universitas Udayana, pp. 31–38 (in Indonesian).

Nkouawa, A., Sako, Y., Li, T., Chen, X., Wandra, T., Swastika, K., Nakao, M., Yanagida, T., Nakaya, K., Qiu, D., Ito, A., 2010. Evaluation of loop-mediated isothermal amplification method using fecal specimens for differential detection of *Taenia* species. J. Clin. Microbiol. 48, 3350–3352.

Palmeri, B., Talamanca, S., Ragonese, P., Aridon, P., Daniele, O., Terruso, V., D'amelio, M., 2011. MRI abnormalities following repeated and incoming seizures. Seizure 20, 90–92.

Rajshekhar, V., Joshi, D.D., Doanh, N.Q., van De, N., Zhou, X., 2003. *Taenia solium* taeniasis/cysticercosis in Asia: epidemiology, impact and issues. Acta Trop. 87, 53–60.

Reeve, D.M., 2010. Comparative Accuracy and "Field Friendly" Effectiveness of Diagnostic Tools for Lymphatic Filariasis and Neurocysticercosis in Papua New Guinea and Timor-Leste with Consideration on the Impact of Parasitic Reduction Programs. JCU ePrints. http://eprints.jcu.edu.au/19042.

Sacchidanand, S., Namitha, P., Mallikarjuna, M., Nataraj, H.V., 2012. Disseminated cutaneous cysticercosis and neurocysticercosis: a rare occurrence. Indian Dermatol. Online J. 3, 135–137.

Sako, Y., Nakao, M., Ikejima, T., Piao, X.Z., Nakaya, K., Ito, A., 2000. Molecular characterization and diagnostic value of Taenia solium low-molecular-weight antigen genes. J. Clin. Microbiol. 38, 4439–4444.

Sako, Y., Itoh, S., Okamoto, M., Nakaya, K., Ito, A., 2013. Simple and reliable preparation of immunodiagnostic antigens for *Taenia solium* cysticercosis. Parasitology 140, 1589–1594.

Sarti, E.J., Schantz, P.M., Lara, R., Gomez, H., Flisser, A., 1988. Taenia solium taeniasis and cysticercosis in a Mexican village. Trop. Med. Parasitol. 39, 194–198.

Sarti, E.J., Flisser, A., Guiterrez, I.O., Lopez, A.S., Plancarte, A., Roberts, J., Schantz, P.M., Wilson, M., 1992. Prevalence and risk factors for Taenia solium taeniasis and cysticercosis in humans and pigs in a village in Morelos, Mexico. Am. J. Trop. Med. Hyg. 46, 677–685.

Sato, M.O., Sako, Y., Nakao, M., Yamasaki, H., Nakaya, K., Ito, A., 2006. Evaluation of purified Taenia solium glycoproteins and recombinant antigens in the serologic detection of human and swine cysticercosis. J. Infect. Dis. 194, 1783–1790.

Schantz, P.M., Kramer, M.H.J., 1995. Larval cestode infections: cysticercosis and echinococcosis. Curr. Opin. Infect. Dis. 8, 342–350.

Schantz, P.M., Wilkins, P.P., Tsang, V.C.W., 1998. Immigrants, imaging, and immunoblots: the emergence of neurocysticercosis as a significant public health problem. In: Scheld, W.M., Craig, W.A., Hughes, J.M. (Eds.), Emerging Infections 2. ASM Press, Washington DC, pp. 213–242.

Simanjuntak, G.M., Margono, S.S., Okamoto, M., Ito, A., 1997. Taeniasis/cysticercosis in Indonesia as an emerging disease. Parasitol. Today 13, 321–323.

Singh, G., Prabhakar, S., Ito, A., Cho, S.Y., Qiu, D., 2002. *Taenia solium* Taeniasis and Cysticercosis in Asia. In: Singh, G., Prabhakar, S. (Eds.), *Taenia Solium* Cysticercosis: From Basic to Clinical Science. CABI Publishing, Oxon, pp. 111–127.

Sudewi, A.A.R., Nuartha, A.A.B.N., 1998a. Neurocysticercosis at Sanglah Central Hospital, Denpasar. In: A paper Presented at the Workshop of and Annual Meeting of Indonesian Neurologist Association, Malang 1-5 July 1998 (in Indonesian).

Sudewi, A.A.R., Nuartha, A.A.B.N., 1998b. Gambaran CT Scan beberapa kasus neurosistiserkosis di Ruman Sakit Umum Pusat Denpasar. In: Working Conference and Annual Scientific Meeting of Indonesian Neurologist Association in 1998 (in Indonesian).

Sudewi, A.A.R., Nuartha, A.A.B.N., 1998c. Neurosistiserkosis di Rumah Sakit Umum Pusat Denpasar. In: Working Conference and Annual Scientific Meeting of Indonesian Neurologist Association in 1998 (in Indonesian).

Sudewi, A.A.R., Aris, G.A., Purba, I.E., Wandra, T., 2013. A case report of neurocysticercosis at Sanglah Hospital, Denpasar, Bali. Indones. J. Infect. Dis. 1, 1–3.

Sudewi, A.A., Wandra, T., Artha, A., Nkouawa, A., Ito, A., 2008. *Taenia solium* cysticercosis in Bali, Indonesia: serology and mtDNA analysis. Trans. R. Soc. Trop. Med. Hyg. 102, 96–98.

Suroso, T., Margono, S.S., Wandra, T., Ito, A., 2006. Challenges for control of taeniasis/cysticercosis in Indonesia. Parasitol. Int. 55, S161–S165.

Sutisna, P., 1993. Sistiserkosis di Bali: iaporan 6 kasus. In: 7th National Seminar Parasitology, Denpasar, Bali (in Indonesian).

Sutisna, P., Kapti, I.N., Wandra, T., Dharmawan, N.S., Swastika, K., Raka Sudewi, A.A., Susilawathi, N.M., Sudarmaja, I.M., Yanagida, T., Okamoto, M., Yoshida, T., Donadeu, M., Lightowlers, M.W., Ito, A., 2019. Towards a cysticercosis-free tropical resort island: a historical overview of taeniasis/cysticercosis in Bali. Acta Trop. 190, 273–283.

Swastika, K., Dewiyani, C.I., Yanagida, T., Sako, Y., Sudarmaja, M., Sutisna, P., Wandra, T., Dharmawan, N.S., Nakaya, K., Okamoto, M., Ito, A., 2012. An occular cysticercosis in Bali, Indonesia caused by *Taenia solium* Asian genotype. Parasitol. Int. 61, 378–380.

Swastika, K., Dharmawan, N.S., Suardita, I.K., Kepeng, I.N., Wandra, T., Sako, Y., Okamoto, M., Yanagida, T., Sasaki, M., Giraudoux, P., Nakao, M., Yoshida, T., Eka Diarthini, L.P., Sudarmaja, I.M., Purba, I.E., Budke, C.M., Ito, A., 2016. Swine cysticercosis in Karangasem district of Bali, Indonesia: an evaluation of serological screening methods. Acta Trop. 163, 46–53.

Swastika, K., Wandra, T., Dharmawan, N.S., Sudarmaja, I.M., Saragih, J.M., Diarthini, L.P.E., Ariwati, L., Damayanti, P.A.A., Laksemi, D.A.A.S., Kapti, N., Sutisna, P., Yanagida, T., Ito, A., 2017. Taeniasis caused by *Taenia saginata* in Gianyar town and *Taenia solium* in Karangasem villages of Bali, Indonesia, 2011–2016: how to detect tapeworm carriers, anamnesis or microscopy? Acta Trop. 174, 19–23.

Torres-Corzo, J., Rodriguez-Della Vecchia, R., Rangel-Castilla, L., 2006. Bruns syndrome caused by intraventricular neurocysticercosis treated using flexible endoscopy. J. Neurosurg. 104, 746–748.

Tumada, L.R., Margono, S.S., 1973. Cysticercosis in the area of the Wissel Lakes, West Irian. Southeast Asian J. Trop. Med. Public Health 4, 371–376.

Wandra, T., Depary, A.A., Sutisna, P., Margono, S.S., Suroso, T., Okamoto, M., Craig, P.S., Ito, A., 2006. Taeniasis and cysticercosis in Bali and North Sumatra, Indonesia. Parasitol. Int. 55 S. 155–S160.

Wandra, T., Ito, A., Yamasaki, H., Suroso, T., Margono, S.S., 2003. *Taenia solium* cysticercosis, Irian Jaya, Indonesia. Emerg. Infect. Dis. 9, 884–885.

Wandra, T., Ito, A., Swastika, K., Dharmawan, N.S., Sako, Y., Okamoto, M., 2013. Taeniases and cysticercosis in Indonesia: past and present situations. Parasitology 140, 1608–1616.

Wandra, T., Sudewi, A.A., Swastika, I.K., Sutisna, P., Dharmawan, N.S., Yulfi, H., Darlan, D.M., Kapti, I.N., Samaan, G., Sato, M.O., Okamoto, M., Sako, Y., Ito, A., 2011. Taeniasis/cysticercosis in Bali, Indonesia. Southeast Asian J. Trop. Med. Public Health 42, 793–802.

Wandra, T., Sudewi, R., Susilawathi, N.M., Swastika, K., Sudarmaja, I.M., Eka Diarthini, L.P., Purba, I.E., Okamoto, M., Budke, C.M., Ito, A., 2016. Neurocysticercosis diagnosed in a patient with Taenia saginata taeniasis after administration of praziquantel: a case study and review of the literature. Primary Health Care 6, 3.

Wandra, T., Swastika, K., Dharmawan, N.S., Purba, I.E., Sudarmaja, I.M., Yoshida, T., Sako, Y., Okamoto, M., Eka Diarthini, N.L.P., Sri Laksemi, D.A.A., Yanagida, T., Nakao, M., Ito, A., 2015. The present situation and towards the prevention and control of neurocysticercosis on the tropical island, Bali, Indonesia. Parasit. Vectors 8, 148.

World Health Organization, 2014. WHO seeks united approach to eliminate tapeworm infection. https://www.who.int/neglected_diseases/cysticercosis?meeting_2014/en/.

Yanagida, T., Yuzawa, I., Joshi, D.D., Sako, Y., Nakao, M., Nakaya, K., Kawano, N., Oka, H., Fujii, K., Ito, A., 2010. Neurocysticercosis: assessing where the infection was acquired from. J. Travel Med. 17, 206–208.

Zhao, J., Lerner, A., Shu, Z., Gao, X., Zee, C., 2015. Imaging spectrum of neurocysticercosis. Radiol. Infect, Dis. 1, 94–102.