MANAGEMENT OF 21 EMERGING LIVESTOCK DISEASES BY THE ISRAEL VETERINARY SERVICES

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ABSTRACT

The threat of terrorism is ever present in Israeli daily life since its establishment in 1948. The possibility of epidemics occurring as a consequence of agro-(bio)-terrorism is a real threat to Israel and therefore discriminating between deliberately introduced and naturally occurring infectious or non-infectious diseases becomes a real concern.

In this review we present twenty-one outbreaks of disease that occurred over the last 30 years and for which epidemiological data were available.

Outbreak	Year of the outbreak
RSF-Reproductive Failure of swine and Exudative Skin Disease in piglets	1994
TGE- Transmissible Gastroenteritis	1990 and 2004
RHD - Rabbit Hemorrhagic Disease	1990
WCS - Weak Calf Syndrome; neonatal calf adenovirosis	2003
Calf intestinal atresia	1999
AHS–Arthrogryposis/Hydranencephaly Syndrome	1969-70 and 2001-03
RP - Rinderpest	1983
LSD- Lumpy Skin Disease	1989, 2006
LHA - Lamb Hemolytic Anemia	1991
PPR - Peste des Petits Ruminants	1993
JHS – Jejunal Hemorrhagic Syndrome	2001
BNVV- Bovine Necrotic Vulvo-Vaginitis	2000
BSE- Bovine Spongiform Encephalopathy	2002
HPAI - Highly Pathogenic Avian Influenza (H5N1)	2006
GNPS - Geese Neuro-Paralytic Syndrome; West Nile Virus infection in domestic geese;	1997
EHDV-7 - Epizootic Hemorrhagic Disease Virus -7;	2006
SA-MCF, Sheep Associated Malignant Catarrhal Fever	2001
BTV-15; Bluetongue Virus -15	2006

Table 1- The twenty-one selected outbreaks and at which year they were recorded

INTRODUCTION

The Israeli livestock industry has experienced many outbreaks of infectious and non-infectious diseases in the last half-century. Located in the Middle East, therefore, discrimination between deliberately introduced and naturally occurring infectious and non-infectious diseases (1) becomes a real concern.

Moreover, Israel is located geographically at the meeting point of three continents, and might be considered as a portal of entry for many "exotic" pathogens introduced by more than 500,000,000 birds that migrate across Israel from north to south, and west to east and vice versa according to the season. In addition, smuggling and illegal transportation of animals that might originate from "exotic" endemic regions, from Africa (Sinai Peninsula) to Asia (Jordan) and back are widespread. This problem is further confounded by the nomadic way of life of the Bedouin who still coexist alongside the industrialized farming system in many areas within Israel, thus creating an epidemiological entity which is often difficult to control.

In this review we present twenty-one outbreaks of disease that occurred over the last 30 years, and for which veterinary epidemiological data are available. The authors also eye-witnessed most of the outbreaks and had participated personally in their investigation.

Zoonotic disease and malicious biocontamination of food (2) are not included in this review.

The following diseases are included (Table 1):

Brief descriptions of outbreaks

Reproductive failure in swine and exudative skin disease in piglets

Swine reproductive failure (RSF) and exudative skin disease in piglets are both clinical manifestations related to porcine parvovirus (PPV) infection in unvaccinated swine populations (3). No clinical cases related to PPV were noted in Israel prior to September 1994.

Brief description of outbreak

In August 1994, 10 pregnant sows, twice vaccinated against PPV with an inactivated vaccine were imported from Cyprus by a closed pig farm located in a semiarid zone. On arrival in Israel, quarantine was imposed for 14 days. After release from quarantine in mid-September, the imported sows were placed in a yard at the farm

that was separated from the adjacent local pregnant sows only by a barbed wire fence. The litters born to the imported sows during September/October were normal, while the reproductive problems initially occurred in the group adjacent to the imported one. In October, local sows farrowed litters of reduced size, and cases of stillbirths, neonatal deaths and mummifications were observed. In total, 60 local sows delivered defective litters through the end of January 1995 (4).

The IVS were notified about this unprecedented malady only at the beginning of February 1995. Due to the clinical manifestations and the pathological findings, PPV was taken as the most probable infectious agent responsible for the outbreak.

Preparedness and response of the diagnostic laboratories and the IVS

The veterinary community in Israel until that time had not experienced any epidemic diseases in the swine industry or had to cope with any kind of outbreak of such a magnitude. Moreover and in parallel, diagnostic laboratories did not possess specific diagnostic tools to confirm the clinical suspicion. For the detection of specific PPV antibodies and PPV antigen, ELISA double antibody sandwich (DAS) and DAS-ELISA (Hispanet, 28230 Las Rozas, Madrid, Spain) commercial kits were purchased by KVI at the end of January 1995. The definitive laboratory diagnosis was delivered to the breeder two days after the arrival of the kits, and the total time had taken approximately 2 weeks.

Diagnosis and confirmation of the etiological agent

All the pathological samples and sera from the affected farm were positive for PPV antibodies and antigens while all pathological materials from control farms were negative (4).

Transmissible gastroenteritis in pigs (TGE)

Transmissible gastroenteritis (TGE) is a contagious disease of pigs that occurs as explosive epizootics. TGE is caused by the TGE virus (TGEV), a member of the family *coronaviridae*. TGEV is a common cause of diarrhea in pigs, affecting all ages but significant deaths occur only in suckling pigs and the severity is related to the age of the infected animals. Almost all susceptible piglets under 10 days of age die within a few days of exposure. When TGEV spreads within a fully susceptible herd with no previous history of infection, up to 100% mortality is expected among newborn pigs, and marked diarrhea and dehydration in weaned pigs. Partial or total agalactia of sows is common (5, 6).

Brief description of outbreak

The Israeli pig industry benefits from a unique epidemiological status. Due to religious customs in the Middle East where the Jewish and Muslim religions prevail, the pig industry is largely isolated, and located far from any area with an intensive pig industry. Consequently, very few epidemics were recorded among Israeli pig herds.

The first cases of diarrhea followed by dehydration and death of piglets, 1 to 7 days old were noted in piggeries on May 7th 2004 where 13 pig herds were raised in northern Israel in a restricted zone of about 1.5 km by 1.5 km. This episode gained epidemic proportions, with mortality as high as 70 to 80% during the first week of life. Two piglets aged 2 days old were brought to the KVI for post-mortem examination on 14th May. Routine histological examination of the small intestine revealed villous atrophy, suggesting the presence of an enteric virus infection.

Preparedness and response of the diagnostic laboratories and IVS

The know-how regarding the pig industry and its various components was negligible due to Jewish and Muslim religious customs. On May 24th, investigators from the KVI visited the affected farms in order to collect pathological and epidemiological data from the suspected TGE outbreak. Although the investigators and the laboratory personnel started from zero, positive laboratory results (using a commercial ELISA kit for the detection of intestinal enteropathogens in calves) confirming coronavirus intestinal infection in piglets was given after one day. Ten days later, the definitive confirmation of swine intestinal coronavirus was made by the Istituto Zooprofilatico di Brecsia (IZS) where pathological specimens had been sent (7).

Diagnosis and confirmation of the etiological agent

Due to the absence of species specific diagnostic tools but assuming that porcine and bovine coronaviruses share common antigenic epitopes, the Bio-X Combined Digestive ELISA Kit (B-6900 Marche-en-Famenne, Belgium), for antigenic detection of rotavirus, coronavirus and F5 in bovine feces was employed (7,8).

Another set of diagnostic procedures was carried out at IZS, using immuno-fluorescence (IFA) on intestinal sections, electron-microscopy (EM) and immuno-EM (IEM) with specific anti-TGEV and the polymerase chain reaction (PCR). This approach was later adopted as a routine diagnostic procedure at the KVI.

The typical findings of villous atrophy and lymphopenia pointed at a probable viral etiology (9). The clinical manifestations and especially the age distribution of the diseased animals, the rapid spread of the disease among the piggeries, its high mortality rate, the antigenic ELISA positive reaction in 63% of the fecal samples submitted to KVI, and the confirmations of serological and antigenic tests from the IZS, lead us to conclude that TGEV was responsible for the outbreak.

Rabbit Hemorrhagic Disease (RHD)

Rabbit Hemorrhagic Disease (RHD) is an acute viral disease in rabbits with high morbidity and mortality, caused by a virus belonging to the *Caliciviridae* family. Although RHD was classified as a notifable disease by the OIE (10), it was not included in the list of notifiable diseases by the IVS.

Brief descriptions of the outbreaks

The first outbreak of RHD occurred in 1990 in an experimental unit for laboratory animals in the Israel Institute for Biological Research with an unprecedented fulminating mortality. More than 43% (12/28) of the rabbits in the unit succumbed within a very short time. The rapidity of the malady and its spread among the caged rabbits, together with and histopathological findings raised the possibility of a viral infection and RHD was suspected. The rabbits had been imported from France (11). The second outbreak occurred in a pets' corner at a school, 17 year later when histopathological findings led the investigators to suspect RHDV infection (12).

Preparedness and response of the diagnostic laboratories and the IVS

The time that elapsed between the observation of the disease and the definitive diagnosis of the 1990 outbreak had taken about 6 months. To the authors' knowledge, no specific reference reagents have been prepared or purchased by the IVS following the first RHD outbreak. The second RHD outbreak was suspected by a junior pathologist employed at the KVI in July 2006. Remarkably, the pathologist to whom this case was assigned was unaware of previous publication of the RHDV outbreak (11), so that the

definitive diagnosis was made only two months later when it was confirmed by a senior pathologist.

Diagnosis and confirmation of the etiological agent

The confirmation of the first Israeli outbreak of RHDV was made by a laboratory experienced with RHDV infections (University of Vienna (13)). The Israeli isolate was confirmed later as belonging to the European group of strains (French) of RHDV (13, 14, 15). The investigators who had suspected RHD infection in July 2006, were not aware about the 1990 outbreak, and wrote erroneously, that the 2006 outbreak "is the first case of RHD in rabbits in Israel". Definitive confirmation came from a laboratory (University of Utrecht) that diagnosed *caliciviruses* routinely (personal communication).

Neonatal calf adenovirosis – weak calf syndrome WCS

A particular polyarthritis (PA) syndrome was observed twice in Israel. It was suggested as one of the multiple features of the weak calf syndrome (WCS) by some American investigators (16, 17). This syndrome is characterized by the appearance of joint swelling, and blood-tinged faeces in very young calves. Koch postulates confirmed that an adenovirus isolated from affected animals that were in a controlled clinical trial was the causative agent of WCS (16).

Brief outbreaks descriptions

The first clinical cases suggested that neonatal calf adenovirosis appeared in Israel in 1995, although no confirmation of the causative agent of this episode was available (18). The first outbreak of PA in newborn calves was brought to our attention in 1995. Its rather rapid mode of spread from farm to farm suggested a viral infection most probably of intrauterine origin. Initially, the affected epicenter comprised 7 large dairy farms and all of them were located around Jerusalem or in the adjacent foothills. The affected calves were usually weak at birth, unable to rise without assistance and when forced to move, walked stiffly suggestive of pain joints. Clinical signs included intra-articular blood-tinged synoviae and the presence of fibrin strands, fresh blood in the feces and eventually massive sub-corneal hemorrhages.

The second similar outbreak of WCS was reported in May 2003, when the local veterinary practitioner noticed that from the first colostral meal immediately after birth, the newborn calves were reluctant to suckle. Clinically, the neonates were unusually weak, unable to rise without assistance and when forced to move, walked stiffly, suggestive of painful joints. Five out of 40 calves died during this episode. On clinical examination the stifle, hock, carpal and tarsal joints were enlarged and on palpation of the adjacent tissues, sub-cutaneous edema and crepitation sounds were felt. From each enlarged joint, about 10 ml of blood-tinged synovial fluid was easily aspirated and fibrin clots appeared shortly after withdrawal. Ecchymotic hemorrhages were noted on the sclera. In several cases a fluid-filled swelling distal to the carpal joint denoted seepage of synovium from the joint cavity. The fresh feces visible on the ground were dotted with drops of fresh blood (19).

Preparedness and response of the diagnostic laboratories and the IVS

The first episode of WCS disappeared spontaneously and no causative agent was identified. With the occurrence of the second similar outbreak, a possible diagnosis was reached. A rapid diagnostic procedure for the identification of bovine adenovirus was unavailable in veterinary laboratories. Therefore, the RIDA® QUICK rotavirus/adenovirus- combi commercial kit (R-Biopharm, AG, Darmstadt, HRB 8321, Gemany) designed for rapid diagnosis of these two human enteric pathogens was applied. The positive results confirmation of our results took an additional 12 months.

Diagnosis and confirmation of the etiological agent

By using the commercial kit RIDA® QUICK rotavirus/adenovirus-combi test we were able to demonstrate the presence of adenovirus in calf feces, synovial fluid and aqueous humor, while fecal samples from healthy calf neonates were negative (19). In order to confirm the suitability of the kit for bovine Adenovirus antigen in calf pathological secretions, the assay was repeated with feces that was seeded with bovine adenoviruses (serotypes 3 and 5) provided by Pálfi, Hungary (19).

Intestinal *atresia* in calves

Intestinal *atresia* (*coli* or/or *ilei*) denoted that an intestinal "cul-de-sac" is formed by two adjacent normally developed intestinal segments. There have been several reports associating the birth of calves with intestinal *atresia* with palpation of the amniotic vesicle during pregnancy before 42 days of gestation (20, 21). These publications had appeared prior to its occurring in Israeli dairy herds in 1999.

Brief outbreak description

In mid-April 1999, *atresia coli* was diagnosed in a newborn calf on post-mortem examination at the KVI. It was then reported that other calves at two adjacent dairy herds located 1 km away did not defecate and had died at the age of 3-4 days [22, 23]. The herds were attended by the same veterinarian.

Preparedness and response of the diagnostic laboratories and IVS

The post-mortem examination, an immediate visit to the affected herds, and especially a search of the literature by the investigators yielded an immediate diagnosis. Moreover, the information provided by the investigators on the iatrogenic nature of this outbreak, avoided the IVS making an unnecessary intervention, such as an imposed quarantine due an unknown etiological agent. The field investigation, the information gathered and the published data were completed in about 2 weeks.

Diagnosis and confirmation of the etiological agent

At necropsy, stasis of the intestinal contents was observed in parts of the intestine. The intestinal "cu-de-sac" segment appeared as a massive swelling anteriorally; while caudally a thin transparent cord without content was identified.

An epidemiological investigation of this outbreak showed a linkage with rectal palpation for early pregnancy diagnosis, performed less than 42 days after insemination. It was calculated that the odds of an affected calf, i.e., one born to a dam that was diagnosed by early palpation as having intestinal *atresia* was 119.7 times higher that one born in normal control herds. A total of 47 calves were born with intestinal *atresia* through mid-2000, out of a total of 682 calves at-risk (22).

The possibilities of genetic involvement (24), infectious agent(s) and/or toxicosis were ruled out. The similarity of this outbreak with the other incidents (20, 21), the characteristic pathological case and the absence of new cases after cessation of early palpation (22), could be considered as a definitive diagnosis.

Congenital abnormalities associated with teratogenic Simbu serogroup virus infections of ruminants

The Israeli ruminants were affected by two defined episodes of neonatal malformation following two arboviral Simbu serogroup infections occurring 35 years apart, in 1969-70 and in 2002-3, respectively (25, 26). Members of the Simbu serogroup of viruses, such as Akabane virus (AKAV), and Aino virus (AINOV) cause epidemics of abnormal parturitions in domestic ruminants, including abortion, stillbirth and birth of deformed calves [27, 28]. The complex is known as the congenital arthrogryposis-hydranencephaly (and hydrocephalus) syndrome (AHS) affecting the musculoskeletal and nervous systems, respectively (29, 30, 31).

Brief outbreaks descriptions

The first recorded outbreak of congenital malformations was in Israeli dairy calves, lambs and kids in 1969/70, and was characterized by the appearance of arthrogryposis and hydranencephaly syndrome (AHS) (25, 32, 33). Based on serological (34), epidemiological [25], clinico-pathological and histopathological findings (32), AHS has been strongly connected with the activity of Akabane virus, and probably also with its principal insect vector in our region, *Culicoides imicola* (30, 35).

The second episode commenced in February 2002, when the first cases of "blind newborn calves" (BNC) appeared in two large neighboring dairy herds in the northern Israel valleys (36). In the following four months, dozens of farms were affected. At necropsy of the calves, the cerebellum appeared normal, while severe micro-hydranencephaly was also observed but arthrogryposis was rarely encountered. Unlike the 1969-70 AHS outbreak, in 2002 outbreak no parallel findings were recorded in sheep or goats. All the clinical cases were confined to the northern valleys of Israel and the 31°00' latitude was the southernmost line of the 2002 epidemic. The same distribution was also noted during the 1969-70 epizootic (25, 36).

The 2002 outbreak persisted until the end of April 2002 suggesting that the circulation of AKAV began in August 2001 and ended prior to November 2001 (36). But, in February 2003, BNC reappeared south of the 31°00' latitude reaching the Arava Rift Valley 400 km south of the 2002 epicenter. Moreover, the 2003 outbreak appeared in areas where it was never recorded previously and that were beyond the southernmost point recorded in the 1969-70 epidemic (25, 36). BNC was found on dairy farms located very close to the Red Sea at 29°30' (36).

Preparedness and response of the diagnostic laboratories and the IVS

The first AHS outbreak in Israel coincided with the similar outbreaks reported in Australia and the Far East (28, 29, 30, 31, 37). So practically the IVS and the KVI laboratories reacted as expected in face of the emerging syndromes (38). Only through collaboration with an expert arbovirus diagnostic laboratory combined with other epidemiological studies and other laboratory assistances, did it become possible to associate AHS with Akabane virus infection. The definitive confirmation of the identity of the causative agent in Israel had taken about 4 years. There were some clinical features of the second episode that resembled the first one and enabled investigators to suspect a possible arboviral infection, but there were three major differences: The first appearance of blind of calves in the semi-arid and arid zones, the almost complete absence of arthrogryposis in cattle (the predominance of the CNS pathology), and the observation that sheep and goats were almost completely spared during the 2002-3 epizootic.

The two waves of the outbreak, met with different states of awareness and therefore preparedness that could be considered as being between an "enzootic disease" and a "(re)-emerging disease" status (38). The main reason for the notification delay which lasted over one month was related to the unfamiliarity of young veterinary clinicians with the clinical manifestations of teratogenic arboviral infections in both cases. This was also true for the diagnostic laboratory personnel. The reestablishment of the diagnostic chain from the farm to diagnostic laboratory based on such experiences took some time. The identification of the causative agent in the latter outbreak was based on serological assays (after their internal and external evaluation). In consequence, confirmation of the causative agent of first episode took about 3 months, while the second one took only less than 2 weeks to confirm.

Diagnosis and confirmation of the etiological agent

The laboratory and epidemiological tools adopted by the Israeli teams to demonstrate the association between congenital malformations in domestic ruminants and AKAV infection during and after the first episode consisted of collecting demographic and seasonal data and investigating the spatial distribution of the affected zones as well the clinical features, description of the macro- and micro-pathology of congenital malformation, the adoption of AKAV SNT in the investigation of the seroreactivity of affected and non-affected farms (zones), to analyze sera of animals that were alive during the epidemics (in the affected zones), and of animals born 3 years after the end of the epizootic (25, 26, 32, 33, 34, 36). Furthermore, it was demonstrated that a bovine fetus of 150 days can amount a specific antibody immune response on antigenic stimulation and that specific antibodies in pre-colostral calf serum have a definitive diagnostic value in identifying the causative agent (39, 40, 41, 42).

The causal agent of the 2002-03 episode was confirmed by findings of AKAV seroreactivity in cattle located in the affected zone, in contrast to none in animals from unaffected farms during the second outbreak (87% and 3.7%, respectively) (36), and by further demonstration and characterization of the Israeli AKAV in C. imicola and in material from aborted fetuses (43, 44).

Lumpy Skin Disease (LSD)

Lumpy skin disease (LSD) presents as an acute, sub-acute or inapparent infectious disease of cattle caused by a single strain of capripox virus known as Neethling virus. LSD is characterized by the rapid eruption of multiple circumscribed skin nodules, generalized lymphadenitis and fever. Other lesions visible at necropsy include necrotic plaques in the membranes, chiefly of the upper respiratory tract, the oral cavity and rumen, and infection may result in mastitis and orchitis (45, 46). Although the field experience and circumstantial evidence suggested that transmission of LSDV occurred primarily by biting insects the mode of field transmission is not fully understood. The results of controlled studies suggested that LSDV transmission between animals by contagion is extremely inefficient, and that parenteral inoculation of virus is required to establish infection (47).

LSDV probably circulates the Middle East, and the first case outside Africa was described in Kuwait in 1986 (48). Since then cases have been confirmed or suspected in the United Arab Emirates, Arab Republic of Yemen, Democratic People's Republic of Yemen (49), and Israel in 1989. The Israeli LSD episode was probably an extension of the Egyptian outbreak (50, 51, 52) while LSDV was also reported in Saudi Arabia in 1992 (53). In 2005-06 an epizootic of LSDV affected 16 provinces in Egypt (54).

Brief description of outbreaks

The first clinical cases in the 1989 outbreak appeared on August

19. The clinical signs spread to additional herds and to two farms in a neighboring village where a local veterinarian had probably transported the secondary outbreak. No clinical description of this outbreak was provided by the authors. Although all the affected herds were slaughtered, only 10% of the animals at risk developed clinical signs (50, 51).

The second occasion on which the IVS intervened in an LSD outbreak began on the evening of 19 June 2006, when a phone call announced the appearance of lumpy urticaria-like lesions in 7 to 10 lactating cows in a large dairy herd. The reappearance of LSD was immediately suspected. The most significant clinical features were the presence of the characteristic bumps that covered the entire skin of the affected cows. All the developmental stages of the lumps were noted from the initial miliary scattered form, namely, the presence of small-localized intradermal lesions, or small intradermal swellings, well developed nodules, very hard on touch, and ensuing sloughing off lesions. Generalized lymphadenopathy could be demonstrated and edematous swelling of the lower gluteal muscles was also noted. The rectal temperature was 40°-41°C (55). One third of the affected dairy herd was affected and therefore was destroyed. One additional confirmed case of LSD occurred in an adult lactating cow on an adjacent dairy farm located within the restricted zone imposed by the IVS.

Preparedness and response of the diagnostic laboratories and the IVS

The clinical diagnosis of the first LSD outbreak was made in 1989 was based on the characteristic clinical signs. The rational given by the authors of this work for the delay in announcing the clinical diagnosis of LSD was related to gross similarity of the lesions with delayed-type anaphylaxis following foot-and-mouth disease vaccination (?), and to the rarity of the disease (45). In contrast, the IVS responded to the second outbreak by establishing a team of veterinary officers and virologists that were ready for an early morning visit to the affected herd. On 20 June 2006 a clinical diagnosis was confirmed one day after the disease was notified to IVS. This happened because two members of the visiting team had been involved both in the diagnosis of the 1989 outbreak (50, 55), and in a controlled clinical trial to assess the efficacy of a sheep-pox vaccine (56). The definitive laboratory confirmation was given by the virology and molecular virology diagnostic laboratories of the KVI within 24 hours of the visit to the affected site.

Diagnosis and confirmation of the etiological agent

The first clinical cases of the 1989 outbreak appeared on August 19 and a clinical diagnosis was made on September 19. The laboratory confirmation was made by EM as no other diagnostic means existed at that time (57). In 2006 while the local practitioner did not suspect the infectious nature of the outbreak for 2-3 weeks, the KVI and IVS experts gave a clinical confirmation of this outbreak immediately, and the definitive antigen of LSDV was confirmed on the following day by the laboratory of molecular virology.

Bovine-colostrum induced anaemia in lambs

This particular form of anaemia of lambs and kids appeared on farms where bovine colostrum was fed in order to increase fecundity and break the transmission cycle of retroviral infection transferred by sheep and goat colostrum to their offspring [58, 59]. The anaemia is caused by the formation of immune complexes on the juvenile erythrocytes. Anti-sheep toxic factors are also present in the colostrum of some cows. This haemolytic anaemia can be easily differentiated form other anemias by finding unique pathognomonic findings of a "pale white bone marrow" in the affected small ruminants (58, 60, 61, 62).

Brief outbreaks descriptions

During the 1991 lambing season, in a flock of Asaf ewes heavily infected with maedi/visna virus, the newborn lambs were immediately separated from their dams and given bovine colostrum. All the lambs given the colostrum died at the age of 8 to 12 days with clinical signs of marked anemia. Lambs were sent to KVI where the pathological diagnosis and hematological results confirmed the clinical findings (63).

Preparedness and response of the diagnostic laboratories and the IVS

When the clinician understood that the intensive medical assistance given to the newborn lambs had failed he attended the necropsy at KVI in person. An expert who acted as the head of a team dealing with the prevention of neonatal ruminant diseases also interviewed the practitioner and raised the suspicion about anemia caused by feeding lambs with bovine colostrum. The marrow of a long bone was then examined and a diagnosis was made. When the instructions given to the farmer were adopted the outbreak immediately ceased.

Diagnosis and confirmation of the etiological agent

The anamnesis and the "pale bone marrow" together with other similar published cases (58, 59, 60, 61, 62, 63) provided sufficient evidence on which to base conclusions about its etiology.

Peste des pe**tits ruminants (PPR)**

PPR is an acute or subacute disease of small ruminants characterized by necrotising stomatitis, enteritis and bronchopneumonia caused by a *Morbillivirus* of the paramyxoviridae family (64). The lesions in the mucosal and lymphoid tissues resemble rinderpest in cattle (65). Evidence of clinical PPR in the Middle East and Egypt suggested that the virus has been circulating in these regions from 1986 onwards (66).

Brief outbreak description

The first clinical signs were observed in an isolated flock of sheep kept in December 1993 and persisted till February 1994. The main clinical features were high fever (41-42°C), watery-bloodstained diarrhea, necrotic lesions on the oral mucosa, and profuse salivation. The mode of transmission of the virus and establishment of the primary infectious site remained unclear as the nearest international borders were at least 100 km to the north and east-north (67).

Preparedness and response of the diagnostic laboratories and the IVS

Faced with the probable entry of PPRV into Israel from neighboring countries, a specific serological test using reference RPV hyperimmune serum was developed in 1984 (68). The clinical acumen of the head of the small ruminant diseases division of the IVS led him to suspect an outbreak of PPR on his first visit to the affected flock, a few days after the appearance of the first signs. Laboratory confirmation of PPV was secured six weeks later.

Diagnosis and confirmation of the etiological agent

As mentioned above, the serological results (67, 68, 69), clinical manifestations (70), and pathological findings were sufficient to confirm the first PPR outbreak in Israel. In addition, PPR antigens were detected in tissues and buffy coat from affected animals and

aborted fetuses (69).

Adult bovine jejunal hemorrhage syndrome (JHS)

The pathognomic clinical features of adult bovine jejunal hemorrhage syndrome (JHS) are defined as acute hemorrhagic enteritis of the small intestine or the hemorrhagic bowel syndrome of adult cattle. The affected cows are often found dead or death ensued within 24 to 36 hours from the onset of clinical signs (85% case fatality rate) (71, 72, 73, 74). The diagnosis is based on the unique post-mortem findings where a section of the jejunum is distended by large amounts of blood or a blood clot that obstructs the intestinal lumen. *Intra-vitem*, non-specific clinical manifestations are observed such as a severe drop in milk production, colic, and abdominal distension.

Brief description of the outbreaks

Three adult dairy cows from three separate farms were necropsied at KVI 2001 because of "sudden death". No specific clinical details were provided, and the owners reported no signs prior to finding the dead cows. On post-mortem examination, extensive hemorrhage and blood clots in the lumen of the small intestine were found. The small intestine of one cow appeared as if the blood "was held" in the upper part since blood was not observed caudally in the colon. The macroscopic and histological examinations of the internal organs as well as routine laboratory examinations revealed no specific disease or pathogens. The cause of death thus appeared to be anemia due to massive intestinal hemorrhage. An additional five cases of "bloody profuse diarrhea" were encountered on three large dairy farms in the south of Israel during January 2002. No other signs were noted other than a marked drop of milk production on the same or previous day to the appearance of the diarrhea. The cows had a normal body temperature. Abdominal colic was the only clinical manifestation and the cows resisted strongly to the penetration of the practitioner's hand during rectal palpation (75).

Preparedness and response of the diagnostic laboratories and IVS

There were only very few publications dealing with this emerging syndrome, and only electronic-library evidence, accessible to KVI personnel, contributed to solve these unknown outbreaks. "Preparedness" was based on professional training alone but there was zero information of such a syndrome.

Diagnosis and confirmation of the etiological agent

The clinical cases examined (and one similar clinical and pathological case in January 1999 that was examined by the KVI) could be considered as probable cases of JHS only retrospectively. No etiological agent(s) has been found so far. The diagnosis was made by comparison of the preliminary findings with those of American investigators who described a newly emerging syndrome, which they tentatively defined as "jejunal hemorrhage syndrome" (JHS) in adult cattle [71, 74].

Bovine necrotic vulvovaginitis (BNVV)

Bovine necrotic vulvovaginitis (BNVV) is characterized primarily by erythema that progresses to hemorrhagic necrosis of the vulvovaginal mucosa. The chronic phase consists of a mucopurulent vaginal discharge. If not treated topically, some cows may develop metritis and/or peritonitis. Systemic treatment has no clinical or bacteriostatic effect on the vulvovaginal lesions (76, 77).

Brief description of the outbreaks

At the end of 2000 and the beginning of 2001, outbreaks of BNVV lasting about 4 months, were observed in three dairy herds in northeast Israel, several months after the introduction of new stock. Heifers and transferred cows were affected more frequently than multiparous and local cows, respectively. Towards the end of 2001, two similar outbreaks of BNVV were reported, one in a previously unaffected herd. The heifers of these herds were transferred as calves to another farm and returned before calving. BNVV was not observed on the host farm. A third outbreak began in January 2002 on a farm that had been affected in the winter of the previous year. After BNVV was described and its putative etiologic agent identified, several sporadic cases were diagnosed on other farms, indicating that it might be under-diagnosed (78, 79).

Preparedness and response of the diagnostic laboratories and IVS

After a delay of several months during which the local veterinarian tried to cope with the episode by himself, the KVI investigators initiated a vast ongoing investigation to clarify the origin of this new syndrome and to differentiate it from being an "exotic" malady. The putative microorganism has been identified, and it seems that the main risk factors associated with BNVV have been identified (78, 79, 80). The estimated time to reach these conclusions took from 4 to 6 months.

Diagnosis and confirmation of the etiological agent

Samples were examined for *Chlamydia* and *Coxiella burnetti*. The only microorganisms cultured consistently from affected cows but not from healthy ones were pigmented, gram-negative, non–sporogenic, anaerobic rods. Autosatellitism was observed in several instances. Identification of the pigmented isolates as P. levii was done according to the Manual of Clinical Microbiology (81). Other potentially pathogenic bacteria have been isolated on occasion, but they could not be correlated with the clinical signs. Isolates of BoHV-4 were also identified by PCR however; subsequent surveys showed that BoHV-4 is not necessary to induce BNVV (77).

Bovine spongiform encephalopathy (BSE): ("Mad cow disease")

Bovine spongiform encepholopathy (BSE) belongs to the transmissible spongiform encephalopathy (TSE) group and affects humans and animals (82). Epidemiological studies in the UK have shown that BSE was caused by contamination of cattle feed with a scrapie-like agent that was found in meat and bone meal (MBM) used as a protein additive in cattle feed (83). BSE became extremely important as a zoonosis because of its apparent link with a new variant of CJD (nvCJD), of which the first 10 cases were reported in 1996 (84).

Brief description of the outbreak

A 10 year old dairy cow from a Kibbutz herd located on the Golan, died on May 20, 2002 following a two-day illness, characterized by a drop in milk yield and nervous symptoms including ataxia, teeth grinding and involuntary chewing movements. The cow had calved twins on May 15, 2002. Because rabies is endemic in this region and in view of the presented nervous signs, a rabies FA test was performed. Samples from the medulla in the obex region were taken for immunoblotting, histopathology and immunohistochemistry (mandatory, see below) (85, 86).

Preparedness and response of the diagnostic laboratories and IVS

The IVS had prepared itself well in advance of the possible introduction of BSE prion into Israel and had therefore, taken some procedural and veterinary precautions:

A ban on the importation of ruminant meat and bone meal (MBM) from the UK since December 1988 (in fact no ruminant MBM

from the UK had been imported to Israel for at least 5 years prior to the ban), a ban on the importation of MBM of mammalian origin from all countries since July 1990. Moreover, a State regulation that bans feeding MBM to (all) farm animals since August 1996 was in place. Consequently, recycling of local mammalian material was discontinued in 1996 (85, 86, 87). A specialist veterinary pathologist and highly skilled laboratory technicians were sent to reference laboratories for training in diagnosing TSE diseases, and BSE in particular. The chief IVS veterinarian issued a decree where it was obligatory to submit any case of ruminant nervous disease for the histopathological diagnosis of TSE.

Personnel from the KVI departments of pathology and immunology, was trained in specialized appropriated laboratory courses on the epidemiology, pathology, and immune techniques of TSE.

Diagnosis and confirmation of the etiological agent

Diagnosis was confirmed by all the diagnostic means available at that time. As the rabies tests were negative, histopathology was performed on the paraffin section of the medulla oblongata of the obex region. Marked spongiform changes in the neuropil of the nucleus of the solitary tact were seen as well as vacuolation in the vagal and olivary nuclei. Immunoblotting using the Prionics-check test was positive for PrPsc and immunohistochemistry for PrPsc using the monoclonal antibody F89/160.1.5 showed marked accumulation of PrPsc in the vagus nuclear complex, the nucleus of the solitary tract and other nuclei of the medulla oblongata. OIE reference laboratories, the University of Bern (Switzerland) and the Veterinary Laboratories Agency, Weybridge (UK) confirmed the KVI results (85). There is no clear explanation for the first and the only BSE case in Israel; and it was therefore, classified as "sporadic". The probable source of contamination (not proved) may have been tallow of European origin that was present in imported calf- milk substitutes.

Highly pathogenic avian influenza (HPAI)

It is not within the scope of this article to discuss the typical signs of HPAI, but for didactic purposes we present the most characteristic features of AI infections that will vary according the virulence of the infecting virus, age and species affected, concurrent diseases, and husbandry at the farm.

The disease appears suddenly, many birds die either without clinical signs or with minimal signs of depression, inappetence, ruffling of feathers and fever. Sick birds sit or stand in a comatose state (head bent downward); the combs and wattles are cyanotic, with edema and or ecchymotic hemorrhages at their tips. Clear respiratory signs are noted and sometimes heard (88).

Brief description of HPAI (H5N1) outbreaks

At two Kibbutz poultry farm located near the border with the Gaza Strip clinical signs and mortality probably related with AIV infections (see above) were noted. Immediate action was taken including animal destruction (89).

Preparedness and response of the diagnostic laboratories and the IVS

This topic is better understood if the chronological events are followed and the more significant milestones in the preparatory process to face the avian influenza (AI) outbreak (H5N1) are highlighted:

7-8/04/2005 - OIE Symposium on H5N1, "global situation and warning". The head of Division of Poultry diseases (KVI) presents Israel.

02/08/2005–Emergency Committee of the Minister of Health organizes a meeting on "AI".

23/8/2005 – IVS assesses the system(s) preparedness (diagnostic ability, monitory status, and links to other governmental systems).

06/09/2005 – IVS establishes an "AI task force".

07/09/2005 – IVS issues an "AI fact sheet" that was mailed to every veterinarian in Israel.

19/09/2005 – The Ministry of Agriculture and Ministry of Health, organizes an open meeting to discuss topics related to AI, in the agriculture sectors and the general public for all those who might be involved in the AI crisis.

27/09/2005 – Ministerial "AI task force" established by the Ministry of Agriculture.

30/10/2005 – IVS makes its own preliminary risk assessment, before the first case diagnosis, and suggestions of how to minimize AI spread from the first infected site.

03/11/2005 – The IVS and the Poultry Marketing Board notified the policymakers about the logistic problems related to "mass poultry destruction".

06/11/2005 – The Government Secretary issues its first decree regarding the possible entry of AI into Israel.

15/11/2005 – Experts from the diagnostic laboratories of the KVI revised all instrumental diagnostic processes and means to face AI diagnosis.

17/11/2005 – The first meeting of the IVS AI task force takes place.

20/11/2005 - Middle East Consortium on Infectious Diseases Surveillance (MECIDS) Regional Pandemic Influenza preparedness meeting convenes.

18/12/2005 – The Israeli Ministry of Defense issues its program to face an AI pandemic episode in Israel.

29/01/2006 – The Civilian Authority of the Samaria-Yehuda-Gaza strip holds a meeting to discuss AI strategy with the Palestinian Authority. Two Israeli tasks forces (Agriculture and Health) presented the Israeli position and the Palestinian authority is presented by its own specialists (Tasks Forces?).

16/03/2006 – In two settlements' (Kibbutzim) poultry farm, near the border with the Gaza Strip an outbreak with clinical signs and mortality probably related with AIV infection was noted. Immediate action started including animal destruction.

19/03/2006 – The poultry diagnostic laboratories of KVI communicated to the head of IVS on the diagnosis of AI H5N1.

In a summary of the March 2006 outbreak, there were 4 infectious sites in the first wave on 16-17/3 and additional 2 infectious sites on 19-20/3 making it a cluster of 6 farms. Then on 23, 26 and 31 of March additional farms were affected, respectively.

The laboratory of (avian) influenza in the KVI possessed almost all the necessary reference reagents for many years, and conducted daily "routine" work with AI viruses (90, 91).

Diagnosis and confirmation of the etiological agent

The ultimate confirmation of the most dangerous scenario, with HPAI H5N1 type came less than 72 hours from of the outbreak.

Sheep associated malignant catarrhal fever (SA-MCF)

Sheep associated malignant catarrhal fever (SA-MCF) is an invariably fatal communicable disease of cattle, caused by the ovine herpes virus-2 (OvHV-2) a gamma-herpes virus (92, 93).

Sheep, and probably goats, are asymptomatic carriers of OvHV-2. Other wild ruminant species might also become infected (94).

MCF appears sporadically, affecting a small number of animals, but OvHV-2 infections can cause epidemics. The most prominent clinical manifestations of MCF are high temperature (41–42° C), abundant and repugnant nasal and/or ocular secretions, hyperventilation and death. However, MCF may appear in many clinical forms, none of which by itself is pathognomic (94). The manifestations vary from a mild, almost unnoticed, form to the multi-organ lesion form accompanied by central nervous system (cerebral) involvement (94). Other forms include the intestinal form of bloody profuse diarrhea, the classical form 'head and eye' (exophthalmus, blindness, photophobia, nystagmus and lacrimation), the respiratory form that comprises lesions of varying degrees in the mouth, larynx, and nose; (intensive redness, ulcerative-necrotic lesions a soft cough, abdominal respiration, head extension, and dyspnoea) [95, 96]. A new rare form of SA-MCF, the cutaneous form, has been recently described [97] in addition to a variety of the intestinal form characterized by a prolapsed rectum (personal observation). The sole definitive diagnosis of MCF virus is to confirm its presence in organs, secretions or blood of the diseased animal (98).

Brief description of the outbreak

Four calves, between 4 and 7 months old, originating from a feedlot farm located at the coastal plain in Israel, were brought for necropsy in May 2001. The farm housed one hundred Israeli Holstein-Friesian calves ranging from 4 to 8 months old that were kept in five adjacent covered yards, according to age groups, and about 20 calves, were allocated to each yard. In an adjacent yard a flock of 50 Awassi sheep, and in another yard a flock of 20 mixed-breed milk goats, was kept under the same roof. One roof covered all the yards, and simple iron grids that did not prevent close physical contact between the different animal species were in place. One of the yards for cattle shared the same drinking and food troughs with the sheep while the other group of cattle shared drinking and food troughs with the goats. Lambs and kids, between 2 and 8 weeks of age were held together with their dams.

The attending veterinarian reported that the initial clinical signs consisted only of one case of profuse diarrhea and some cases of ocular lacrimation, with a high temperature of 42°C. The sick calves died within 3–7 days within the appearance of the initial clinical signs. Necropsy of the four calves revealed no specific gross lesions, while one showed mild abomasal hemorrhages. Four cases of the head and eye form were observed 1 week later. One calf, otherwise without additional signs, showed incoordination and neck stiffness, suggestive of the nervous form. These were the first clinical signs suggestive of MCF. At the same time the first histopathological examination showed obliterative arteriopathy in the brain. A tentative diagnosis of MCF was advanced. During the next 3 months, 30 additional calves became ill at the rate of one to four calves per week, and all of them died. Most of the initial cases were the head and eye form, but some of them progressed to other forms, so as the epidemic progressed, typical manifestations of the respiratory, intestinal and nervous forms were all encountered (99, 100).

Preparedness and response of the diagnostic laboratories and the IVS

Although, theoretically MCF was known to our professional stuff, the possibility that SA-MCF diagnosis was probably underestimated in Israel and elsewhere, could be deduced from the IVS epidemiological bulletins reporting communicable diseases. The last SA-MCF case reported by the IVS before this episode was in 1991, and it seems unlikely that Israel was free of SA-MCF in the interim period. Moreover, seventeen cases of MCF were diagnosed in the first 6 months following the 2001 outbreak. Most of these cases were sent to the KVI for diagnosis of CNS symptoms such as rabies and listeriosis (100). The classical diagnostics procedures, based on the characteristic histopathological pictures was used. The newer PCR methods was adopted in this case and the hemi-nested PCR for the detection of OvHV-2 sequences was conducted by the two-step amplification reaction cycle.

It is documented that PCR was in use elsewhere from 1993 onwards (98).

Diagnosis and confirmation of the etiological agent

Organs were fixed in 10% neutral buffer formalin and prepared for histopathological examination. As mentioned above, the histopathological findings were suggestive of MCF. But a definitive diagnosis was conducted, and the reagents were externally evaluated by two experts. This process lasted more than one year.

Bluetongue virus 15 infection

Brief description of outbreak

Typical bluetongue symptoms were observed in November 2006 in an Assaf and mixed flock of 450 sheep located on the fringe of the Negev Desert. The animals presented the typical edematous head, ulcerative lesions in the oral cavity and interdigital tegument. The typical "dancing sheep" and the "kisses" left no doubt about the etiology. The mortality was very high, and 64 deaths were recorded in less than 7 days. The exact number of diseased animals was estimated to be between 50% and 60%. This episode was very unusual in our region; the outbreak erupted in one flock and none of the many other flocks around was affected in the vicinity. The BTV affected a rather resistant breed with clinical manifestations of the BTV endemic strains. Moreover, for at least 15 years all the recorded clinical signs, if presented, were very sporadic. We attributed the lack of BT outbreaks to the fact that Israeli sheep breeds are relatively resistant to all five endemic serotypes BTV-2, 4, 6, 10 and 16. We therefore suspected the emergence of an exotic strain, and the suspicion was confirmed within a few days, because all the BTV seroassays available at the KVI reacted negatively. Additional unusual signs were also noted; the cattle herd, on the same farm, located only a few meters from the sheep pens, was unaffected. Also, the distribution of affected animals within the flock was very unusual. In one pen most of the deaths and symptoms occurred, while in the next pen, separated by a simple fence, there were few deaths, there were pens with no mortality and in one pen all the animals were apparently healthy. Surprisingly, no age-related attack pattern could be discerned.

Diagnosis and confirmation of the etiological agent

The virus was identified as BTV serotype 15 (BTV-15) from infected eggs cultivated at the KVI diagnostic laboratory by the UK reference laboratory at Pirbright. This was confirmed antigenically (PCR) and serologically (SNT) with sera provided from the KVI (101).

Preparedness and response of the diagnostic laboratories and the IVS

KVI and IVS monitor BTV presence in Israel on a regular basis, by conducting serological surveys passively and actively. Most of the field veterinary officers are familiar with the classical BT symptoms and recognize them from time to time- 2 to 4 cases each year. For this reason an exotic strain was immediately suspected although no specific reference reagents were available. The appropriate laboratory assays initiated by the KVI aided the rapid

definition by the BT reference laboratory.

West Nile disease of domestic geese (Goose neuroparalytic syndrome GNPS)

West Nile virus is transmitted by mosquitoes of the *Culex* spp and is the casual agent of West Nile fever (102). A variant isolate Isr98/NY99 was able to infect flocks of young domestic geese between 3 and 10 weeks old (102). Many species of wild and captive birds are also affected, while geese are the only domestic avian species that succumb to WNV infection. Israeli goose farms were decimated by the disease between 1997 and 2001 (103, 104, 105).

Brief description of outbreaks

The fist outbreak in geese was notified in the fall of 1997 as a characteristic neuroparalytic syndrome of flocks between 5 and 9 weeks of age. Goslings as old as 11 weeks also were affected, and virus neutralizing antibodies were found (106).

Preparedness and response of the diagnostic laboratories and IVS

Three distinct KVI laboratories had their specific reference reagents prepared in advance as the "WN epidemic" was an ongoing fact at these times (105).

Diagnosis and confirmation of the etiological agent

The definitive diagnosis was made available in less than 2 weeks from the date that IVS was notified and suspected materials reached the KVI laboratories. WNV was isolated from the brains of sick geese by inoculating the yolk sacs of embryonated chicken eggs at day 7 of inoculation with a goose brain homogenate. All the procedure including immunofluorescence and PCR confirmation lasted approximately 3 months.

Epizootic hemorrhagic virus infection in cattle

The hemorrhagic syndrome caused by epizootic hemorrhagic virus (EHDV) infection of cattle was first described as follows: 10-20% reduction in milk production, partial anorexia, reduced rumination, short-term low fever (101, 107). Additional signs included a marked serous to purulent nasal discharge, excessive salivation, nasal and lip redness, with scaling and tongue swelling, cyanosis and erosions, petechia on the tips of the lingual and buccal papillae similar to those noted in several other hemorrhagic syndromes in ruminants (108). Ocular lesions might be noted and they appear as epiphora, conjunctival hyperemia and palpebral edema. Some cases of stiff gait, muscle tremors of the appendages and recumbency were also noted. Several animals exhibited red to purple discoloration of the udder and hoof edema with echymotic hemorrhages (101, 107).

Brief description of the outbreak

The IVS was notified of a novel disease syndrome, on September 5, 2006. However, the first clinical signs were seen toward the end of August 2006. The outbreak was first reported from several dairy farms located in the southern Jordan River Valley in Israel (part of the Rift Valley). This first reports described decreased milk production of 10-20% and partial anorexia, followed by clinical signs of reduced rumination, low rise of fever of short duration, weakness and stiff gait. In addition, prominent serous to purulent nasal discharge, excessive salivation, and nasal and lip redness with scaling and tongue swelling cyanosis and erosions were observed, petechia on the tips of the lingual and buccal papillae were similar to those noted in several ruminant hemorrhagic syndromes (108). Ocular lesions appeared in some animals as epiphora, conjunctival hyperemia and palpebral edema. Also evident in some animals were a stiff gait, muscle tremors of the appendages and in some cases recumbency. Several animals appeared with red to purple discoloration of the udder and hoof edema with echymotic hemorrhages. Not all of the above mentioned clinical signs were seen on the same farm. Throughout, the following weeks, the disease outbreaks extended northwards and southwards in the Jordan Valley into the Upper Galilee and the Dead Sea area, while from the beginning of October the disease spread westward to dairy farms in the Jezre'el Valley and the Golan heights. Several foci appeared in the Mediterranean coast plain. A total of 105 cattle herds were involved, 80 of the affected were dairy, 21 beef and 4 feedlots. Morbidity rate within herd was from 5% to 80% of milking cows with varied involvement of replacement heifers. The mortality rate was very low. The duration of the disease in affected animals was reported to range between 3 to 30 days. There were no reports of a distinctive disease syndrome in sheep or goats in these areas (101, 107).

Hemorrhagic diseases that are caused by Orbiviruses are seasonal since their vector might be some blood suckling insects, as is the case of BTV which is transported in our region by *Culicoides imicola* (109). However, the source and the vector of the EHDV is still unknown.

Preparedness and response of the diagnostic laboratories and the IVS

Laboratory investigations: the first samples were tested for BEF and BT by PCR and virus isolation in embryonated chicken eggs. Since EHD was never seen in Israel nor in the region, no diagnostic procedures were readily available therefore, samples were sent to the BT reference laboratory at Pirbright, UK.

Not only were the specific reagents unavailable at the diagnostic laboratories of the KVI but this outbreak found the personnel in total initial confusion.

Diagnosis and confirmation of the etiological agent

Of the total 31 samples sent, 11 were confirmed positive for EHD virus- type 7 by PCR while all samples were BTV negative. These results were from 15 farms of which 10 were positive for EHDV, and in addition, results were confirmed by the detection of specific EHDV (107) antibodies by ELISA.

Although all the systems were unprepared, the definitive causative agent was confirmed after approximately one month by using external help and intellectual agility.

Rinderpest

Rinderpest (RP) is caused by a negative-strand RNA virus of the *Morbillinirus* genus, family *Paramyxoviridae*. The classical description of RP refers to it as a highly fatal disease of domestic cattle, buffalo and yaks. Also the virus affects small domestic ruminants and a variety of wildlife species within the order *Artiodactyla* . The disease is characterized by pyrexia, the progressive development of mucopurulent ocular and nasal discharges and high morbidity and mortality. Digestive tract involvement is marked by the development of diarrhea and dysentery. If rinderpest is suspected, particular attention should be paid on post-mortem examination to the abomasums, which may be engorged, and the Peyer's patches which lymphoid necrosis.

Reports of RP in the Palestine Mandate go back to 1927, and when it appeared in the Middle East in 1970-71, the entire cattle population in Israel was vaccinated against RP. Vaccination was repeated in February-March 1982 only in the northern regions of Israel due to its reappearance in the Middle East.

Brief descriptions of outbreaks

In early 1982, a RP outbreak was reported in a small herd of local beef cattle near the northern border of Israel. Subsequently 3 additional foci were reported at the same time in herds of beef cattle. All these herds were either partially or totally unvaccinated (114). Dairy cattle and small ruminants were not affected in this outbreak. In six partially vaccinated beef herds the mortality rate reached 70 to 90% whereas in 3 completely vaccinated beef cattle herds it was between 6 and 16%.

Anorexia, an elevated body temperature of 40-42°C, excessive salivation with fetid odors, diarrhea and dysentery were the major visible clinical signs of the affected animals. A mucosal disease was noted. Mortality ensued within 24-48 hours of the onset of the clinical signs in some peracute cases.

Preparedness and response of the diagnostic laboratories and the IVS

In 1970-71 due to the presence of RP in the Middle East, a general vaccination was carried out in Israel as a precautionary measure. Information regarding the appearance of RP in countries surrounding Israel reached the IVS through OIE alerts, publications in February-March 1982 and information provided directly to the IVS by the breeders along the Lebanese border about an unusual disease presence in Lebanon. In consequence, the cattle in the northern sector of Israel and its northern borders were vaccinated against RP and movement of cattle and small ruminants in these regions was completely prohibited.

The unusual mortality in beef cattle herds near the Lebanese border was recognized promptly and relevant samples were shipped immediately to KVI. Statutory regulations, such as the disposal of affected herds, and confiscation and destruction of livestock transported without special permission. In February 1984, 7 months after the last outbreak of RP, Israel was declared free of RP.

Diagnosis and confirmation of the etiological agent

The first diagnosis was based on the characteristic clinical signs, gross pathological changes, and the geographical appearance of the first focus of disease. The virological assays carried out in the diagnostic viral laboratory where isolation of the virus corroborated the clinical diagnosis (114).

DISCUSSION

When a mass outbreak of a disease or an unusual event affecting animal health occurs, it is extremely important to determine whether an infectious (or contagious), transmissible agent is involved. Mass toxicosis or/and iatrogenic (deliberate or not) causes must be included. Some authors have used markers to help discern between deliberate, malicious and natural (infectious) causes (1).

In this paper we have presented various epidemics of different natures, fortunately none of them were deliberate, but which could potentially become terrorist acts. Most of the presented outbreaks are of an infectious origin, some pose an immediate global concern such as are the HPAI (N5H1) and WNV diseases. Few pose a regional risk and are represented by the vector-born infections such as the LSDV, BTV and EHDV infections (Rift Valley Fever virus and Bovine Ephemeral virus were not included in this paper). There are outbreaks triggered by field veterinarians or by the animal breeders. These are represented by the calf intestinal *atresia* and hemolytic anemia in lambs. In these two last two syndromes an immediate process of investigation must be carried out because they might resemble infectious disease, and if not promptly diagnosed as such, could carry a heavy unnecessary burden and cost on the reference diagnostic laboratory and probably would lead to incorrect conclusions.

It was interesting to compare the examples of reemerging diseases that have appeared twice. The AKAV infection appeared in 1969-70 and in 2001-02. The causative agent was elucidated in the first episode by a foreign diagnostic laboratory approximately 4 years after the clinical features of the epidemic were described. The second episode was confirmed also by the same laboratory, because the local laboratory raised the possibility of a Simbo serogroup infection. The partial dependence on external help might be the reason for a shorter elapsed time between the second outbreak and the confirmation of the same causative agent. Knowledge of arthrogryposis/hydran/microencephaly is a good example why professional preparedness is a favorable factor although it is not reflected in this work. The same but more significantly concerns the two separate outbreaks of LSD. Because one of the authors was involved in the diagnosis of the first episode of 1989, the second outbreak was clinically diagnosed on the spot and confirmed by PCR in less than 24 hours. The reemergence of LSD, that to date (August 2007), affects many settlements along the Gaza Strip, is an example of the difficulty of the IVS to control an epidemic due to the lack of veterinary infrastructure across the border, and the complete separation between the two neighboring veterinary services, therefore, could be considered a form of agro-terrorism.

The RHD outbreak is a good example of what happened when the system learnt nothing from an emerging situation and why it is important to transmit intellectual property between generations. Although, the fist outbreak was published and one of the pathologist stuff was employed at the times at the KVI, a new stuff member failed to suspect the second case although death rabbits were submitted for post- mortem examination. This happened because no records of the first RHD outbreak were kept.

There are few syndromes with a strict local connection. The BNVV disease was extensively and exclusively described in Israel. Can this outbreak bear a massage for others, indicating an epidemic elsewhere? Does environmental destabilization might be a cause of such health consequences on animals that suffered stressful movement and mixing with other populations.

We think that this work might also serve as a lever for the policy makers placed "in the high windows" responsible for the allocation of necessary resources, and provides also an umbrella under which the process of preparedness transpires.

In Israel the same vision is also shared by investigators dealing with zoonotic diseases in thee human medicine field, and considering that most agents with bioterrorism potential are zoonotic (111).

Field Epidemiology training Program (FETPs) sponsored by the U.S. Center for disease Control Prevention (CDC) have provided training for (local) epidemiologist as the Organization's World Health Report (112). Lescano et al., [113] have reported that graduates from these CDC courses, participated in more outbreaks investigation after training (0.2 vs. 0.9 investigations per trainee-year $P<0.001$).

This seems to be a powerful tool for ameliorating what we define as "professional preparedness": Veterinary Medicine needs such

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Cover image - Rock hyrax

The hyrax is 30 to 70 cm long and weighs between 2 and 4.5kg, Male hyraxes are slightly larger than females. The hyrax gives birth to two to four young after 6 to 7 months gestation period. The young are well developed at birth with fully-opened eyes and a complete pelage. The young can ingest solid food after two weeks and are weaned at ten weeks. They are sexually mature after 16 months, and reach adult size at three years. Their typical lifespan is about ten years.

Hyraxes are found in Africa and the Middle East. In Israel they are found mostly on the Hermon and the Carmel, in the Judean desert and the Negev. Hyraxes live in family groups of up to 100 individuals.

Hyraxes have poorly developed body temperature regulation and compensate by basking in the sun like reptiles.

Hyraxes are sometimes described as being the closest living relative of the elephant. This is because they shared a common ancestor in the distant past when hyraxes were larger and more diverse. However, the details of this relationship remain open to debate.