HEPATITIS B VIRUS (HBV)

Animal Group(s) Affected	Transmission	Clinical Signs	Severity	Treatment	Prevention and Control	Zoonotic
Primates, esp. gibbons, wooly monkeys, chimpanzees, humans; also rodents, birds	Transmitted vertically (perinatal) or horizontal (percutaneous or mucosal exposure to infected body fluids, i.e. blood, saliva, sexual fluids, wound exudate)	Weight loss, lethargy, anorexia, icterus, abdominal discomfort, nausea, vomiting	Often asymptomatc in non-human primates but can cause severe disease in gibbons and wooly monkeys; increased prevalence of hepatocellular carcinoma in chronic infections in woodchucks, humans.	Supportive care; antivirals or α-interferon can be attempted but to date unsuccessful in animal cases.	Human recombinant vaccine should be considered for non-exposed primates	Assumed but unproven

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Susceptible animal groups: Hepadnaviruses are divided into two genera: Orthohepadnavirus in mammals; Avihepadnavirus in birds. Orthohepadnavirus infect humans, apes, and rodents. Human Hepatitis B viruses consists of at least 8 genotypes (A through H, recently also I and J) with each divided into several sub-genotypes. Non-human primate hepatitis B viruses infect gorillas (gorilla hepatitis B virus), chimpanzees (chimpanzee hepatitis B virus), orangutans (orangutan hepatitis B virus), gibbons (gibbon hepatitis B virus), and woolly monkeys (woolly monkey hepatitis B virus). Rare or experimental in other primates (macaques, baboons, spider monkey, vervet monkey, and ruffed lemurs). Hepadnaviruses also infect woodchucks (woodchuck hepatitis virus), ground squirrels (ground squirrel hepatitis virus), and arctic squirrels (arctic ground squirrel hepatitis virus). Avihepadnaviruses infect birds, including ducks, geese, herons, storks, cranes. Woodchucks, chimpanzees, and ducks are used as experimental models for hepatitis B in humans.

Causative organism:

Orthohepadnaviruses (Mammals)

- Human hepatitis B virus (at least 8 genotypes each with several sub-genotypes)
- Gorilla hepatitis B virus (GoHBV)
- Chimpanzee hepatitis B virus (ChHBV)
- Orangutan hepatitis B virus (OuHBV)
- Gibbon hepatitis B virus (GiHBV)
- Woolly monkey hepatitis B virus (WMHBV)
- Woodchuck hepatitis virus (WHV)
- Ground squirrel hepatitis virus (GSHV)
- Arctic ground squirrel hepatitis virus (ASHV)

Avihepadnaviruses (Birds)

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- Duck hepatitis B virus
- Heron hepatitis B virus
- Stork hepatitis B virus
- Crane hepatitis B virus
- Ross' goose hepatitis B virus
- Snow goose hepatitis B virus
- Parrot hepatitis B virus

Zoonotic potential: Transmission of nonhuman primate hepatitis B viruses to humans is in theory possible although yet unproven; transmission of human HBV infection to non-human primates is well documented. All primate and veterinary staff in zoos should consider vaccination against HBV.

Distribution: Multiple species and subspecies-specific and regional variants exist, but many are thought to cross-infect other species, although further epidemiologic and molecular studies ongoing and needed. Recombination between ape variants has been proven. Infection has been shown in free-ranging chimpanzee, gorilla, orangutan, and gibbon populations.

Incubation period: 45-120 days or more

Clinical signs: Infection can result in:

1. Acute transient or fulminant hepatitis, with fever, anorexia, lethargy, nausea, vomiting, icterus, abdominal discomfort, ascites. Increases in alanine transferase (ALT) and aspartate aminotransferase (AST) documented in several species.
2. Asymptomatic infection or mild disease and clearance of the virus with lifelong immunity.
3. Chronic hepatitis leading to liver failure or hepatocellular carcinoma. Increases in ALT and AST possible.

Post mortem, gross, or histologic findings: Hepatitis, hepatic necrosis, hepatic fibrosis is seen in humans, gibbons, and wooly monkeys, but rarely in other primates. Chronic infections can lead to hepatic cirrhosis and hepatocellular carcinoma in humans as well as in woodchucks, to a lesser degree in ground squirrels and ducks, but has not been reported in non-human primates. More cases with histologic and clinical disease may become evident as non-human primates diagnosed only in the past few decades age and develop chronic disease.

Diagnosis: Increased ALT and AST on biochemical analysis. Since the genome of human and non-human primate hepatitis B viruses are similar, human Hepatitis B testing is applicable in non-human primates as follows:
HBsAg+ and HBsAB- indicates active, acute or chronic infection;
HBsAg- and HBsAB+ indicates exposure but clearance of virus and natural immunity (or vaccination);
HBcAg+ indicates acute infection (< 6 mo);
HBcAB+ indicates acute or chronic infection; indicates previous exposure or chronic infected carrier status;
HBeAg+ indicates active virus production and infectivity;
HBeAg+ and HBeAB- indicates active virus production and high infectivity;
HBeAg- and HBeAB+ indicates no viral shedding and typically a predictor of long-term clearance of virus, but still potentially infectious in some cases;.
PCR testing also available and indicates infectivity if positive.

Material required for laboratory analysis: Serum for liver enzyme analysis and serology testing; serum or whole blood EDTA or ACD for PCR testing.

Relevant diagnostic laboratories:
VRL Labs
P.O. Box 40100
7540 Louis Pasteur, Suite 200

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San Antonio, Texas 78229
877-615-7275
HBsAg, HBsAB, HBcAB: 0.5-1.0 ml serum for each test required
Hepatitis B PCR: 2 ml fresh EDTA or ACD whole blood or 1 ml frozen serum/plasma

BioReliance Laboratory Animal Diagnostic Services
14920 Broschart Rd.
Rockville, MD 20850
800-804-3586
HBsAg, HBcAB: 0.5-1.0 ml serum;
PCR: 2-3 ml fresh EDTA whole blood

Zoologix, Inc.
9811 Owensmouth Ave, Suite 4
Chatsworth, CA 91311
818-717-8880
HBsAB (ELISA): 0.5 ml serum/plasma
PCR: 0.5 ml EDTA or ACD whole blood

Treatment: Supportive care, no specific treatment proven in non-human primates. In humans, tenofovir or entecavir and other nucleoside analogs antivirals or α-interferon are given if high HBeAg+ and DNA+ and increased ALT (chronic active hepatitis). In humans, antivirals suppress the virus but do not provide a cure, while α-interferon cures a low percent of those treated for 1 year. Lamivudine and α-interferon have been attempted in limited cases in chimpanzees and woodchucks, respectively, without signs of improvement.

Prevention and control: Screen colony once and new animals at preshipment or quarantine exam with HBsAg or PCR. Avoid adding positive breeding animals to negative and unvaccinated groups. Vaccination can be used to protect negative (HBsAB- or PCR-) animals if exposed to positive animals. Two recombinant vaccines are currently available in the US in humans (Engerix B and Recombivax HB) and given at 0, 1, and 6 months with life-long immunity in humans.

Suggested disinfectant for housing facilities: 1:10 bleach; The virus can survive up to 7 days even on surfaces contaminated by dried blood/bodily fluids.

Notification: None

Measures required under the Animal Disease Surveillance Plan: N/A

Measures required for introducing animals to infected animal: Animal to be introduced should be tested, if (HBsAg- or PCR- and HBsAB-), animal should be vaccinated before introducing to positive (HBsAg+ or PCR+) animal.

Conditions for restoring disease-free status after an outbreak: Area should be completely cleaned and disinfected. All animals should be tested with HBsAg or PCR and HBsAB to determine status. Animals that are HBsAg- or PCR- and HBsAB- should be immunized.

Experts who may be consulted:

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References

1. http://www.cdc.gov/hepatitis/HBV/index.htm (for more details on test interpretation see: http://www.cdc.gov/hepatitis/HBV/PDFs/SerologicChartv8.pdf) Accessed 2 July 2013.
2. Heckel, J.O., W. Rietschel, and F. T. Hufert. 2001. Prevalence of hepatitis B virus infections in nonhuman primates. J. Med. Primatol. 30:14-19.
3. Lanford, R. E., D. Chavez, K. M. Brasky, R. B. Burns, and R. Rico-Hesse. 1998. Isolation of a hepadnavirus from the woolly monkey, a New World primate. Proc. Natl. Acad. Sci. 95: 5757-5761.
4. Lyons, S., C. Sharp, M. LeBreton, C. F, Djoko, J. A. Kiyang, F. Lankester, T. G. Bibila, U. Tamoufé, J. Fair, N. D. Wolfe, and P. Simmonds. 2012. Species association of hepatitis B virus (HBV) in non-human apes; evidence for recombination between gorilla and chimpanzee variants. Plos One7: 1-9.
5. Njouom, R, S. A. S. Mba, E. Nerrienet, Y. Foupouapouognignia, and D. Rousset. 2010. Detection and characterization of hepatitis B virus strains from wild-caught gorillas and chimpanzees in Cameroon, Central Africa. Infect. Genet. Evol. 10: 790-796.
6. Sa-Nguanmoo, P, P. Rianthavorn, S. Amornsawadwattana, and Y. Poovorawan. 2009. Review: Hepatitis B virus infection in non-human primates. Acta Virol. 53: 73-82.
7. Thornton, S. M., S. Walker, and J. N. Zuckerman. 2001. Management of hepatitis B virus infections in two gibbons and a western lowland gorilla in a zoological collection. Vet. Rec. 149: 113-115.