

The h/h blood group, also known as Oh or the Bombay blood group, is a rare blood type. This blood phenotype was first discovered in Bombay, now known as Mumbai, in India, by Dr. Y. M. Bhende in 1952. It is mostly found in South Asia (India, Bangladesh, Pakistan) and parts of Middle East such as Iran. Problems with blood transfusion The first person found to have the Bombay phenotype had an interesting blood type that reacted to other blood types in a way never seen before. The serum contained antibodies that reacted with all red blood cells' normal ABO phenotypes. The red blood cells appeared to lack all of the ABO blood group antigens and to have an additional antigen that was previously unknown. Individuals with the rare Bombay phenotype (hh) do not express H antigen (also called substance H), the antigen which is present in blood group O. As a result, they cannot make A antigen (also called substance A) or B antigen (substance B) on their red blood cells, whatever alleles they may have of the A and B blood-group genes, because A antigen and B antigen are made from H antigen. For this reason people who have Bombay phenotype can donate red blood cells to any member of the ABO blood group system (unless some other blood factor gene, such as Rh, is incompatible), but they cannot receive blood from any member of the ABO blood group system (which always contains one or more of A, B or H antigens), but only from other people who have Bombay phenotype. Receiving blood which contains an antigen which has never been in the patient's own blood causes an immune reaction due to the immune system of a hypothetical receiver producing immunoglobulins not only against antigen A and B, but also against H antigen. The most common immunoglobulins synthesized are IgM and IgG (and this seems to have a very important role in the low frequency of hemolytic disease of the newborn among non-Bombay offspring of Bombay mothers). It is very important, in order to avoid any complications during a blood transfusion, to detect Bombay phenotype individuals, because the usual tests for ABO blood group system would show them as group O. Since Anti-H immunoglobulins can activate the complement cascade, it will lead to the lysis of red blood cells while they are still in the circulation, provoking an acute hemolytic transfusion reaction. This, of course, cannot be prevented unless the lab technologist that is involved is aware of the existence of the Bombay blood group and has the means to test for it. Incidence This very rare phenotype is generally present in about 0.0004% (about 4 per million) of the human population, though in some places such as Mumbai (formerly Bombay) locals can have occurrences in as much as 0.01% (1 in 10,000) of inhabitants. Given that this condition is very rare, any person with this blood group who needs an urgent blood transfusion will probably be unable to get it, as no blood bank would have any in stock. Those anticipating the need for blood transfusion may bank blood for their own use, but of course this option is not available in cases of accidental injury. For example, by 2017 only one Colombian person was known to have this phenotype, and blood had to be imported from Brazil for a transfusion. Biochemistry Biosynthesis of the H, A and B antigens involves a series of enzymes (glycosyl transferases) that transfer monosaccharides. The resulting antigens are oligosaccharide chains, which are attached to lipids and proteins that are anchored in the red blood cell membrane. The function of the H antigen, apart from being an intermediate substrate in the synthesis of ABO blood group antigens, is not known, although it may be involved in cell adhesion. People who lack the H

antigen do not suffer from deleterious effects, and being H-deficient is only an issue if they need a blood transfusion, because they would need blood without the H antigen present on red blood cells. The specificity of the H antigen is determined by the sequence of oligosaccharides. More specifically, the minimum requirement for H antigenicity is the terminal disaccharide Fucose-Galactose, where the fucose has an $\alpha(1-2)$ linkage. This antigen is produced by a specific fucosyl transferase that catalyzes the final step in the synthesis of the molecule. Depending upon a person's ABO blood type, the H antigen is converted into either the A antigen, B antigen, or both. If a person has group O blood, the H antigen remains unmodified. Therefore, the H antigen is present more in blood type O and less in blood type AB. Two regions of the genome encode two enzymes with very similar substrate specificities: the H locus (FUT1) which encodes the Fucosyl transferase and the Se locus (FUT2) that instead indirectly encodes a soluble form of the H antigen, which is found in bodily secretions. Both genes are on chromosome 19 at q.13.3. - FUT1 and FUT2 are tightly linked, being only 35 kb apart. Because they are highly homologous, they are likely to have been the result of a gene duplication of a common gene ancestor. The H locus contains four exons that span more than 8 kb of genomic DNA. Both the Bombay and para-Bombay phenotypes are the result of point mutations in the FUT1 gene. At least one functioning copy of FUT1 needs to be present (H/H or H/h) for the H antigen to be produced on red blood cells. If both copies of FUT1 are inactive (h/h), the Bombay phenotype results. The classical Bombay phenotype is caused by a Tyr316Ter mutation in the coding region of FUT1. The mutation introduces a stop codon, leading to a truncated enzyme that lacks 50 amino acids at the C-terminal end, rendering the enzyme inactive. In Caucasians, the Bombay phenotype may be caused by a number of mutations. Likewise, a number of mutations have been reported to underlie the para-Bombay phenotype. The Se locus contains the FUT2 gene, which is expressed in secretory glands. Individuals who are "secretors" (Se/Se or Se/se) contain at least one copy of a functioning enzyme. They produce a soluble form of H antigen that is found in saliva and other bodily fluids. "Non-secretors" (se/se) do not produce soluble H antigen. The enzyme encoded by FUT2 is also involved in the synthesis of antigens of the Lewis blood group. Genetics Bombay phenotype occurs in individuals who have inherited two recessive alleles of the H gene (i.e.: their genotype is hh). These individuals do not produce the H carbohydrate that is the precursor to the A and B antigens, meaning that individuals may possess alleles for either or both of the A and B alleles without being able to express them. Because both parents must carry this recessive allele to transmit this blood type to their children, the condition mainly occurs in small closed-off communities where there is a good chance of both parents of a child either being of Bombay type, or being heterozygous for the h allele and so carrying the Bombay characteristic as recessive. Other examples may include noble families, which are inbred due to custom rather than local genetic variety. Hemolytic disease of the newborn In theory, the maternal production of anti-H during pregnancy might cause hemolytic disease in a fetus who did not inherit the mother's Bombay phenotype. In practice, cases of HDN caused in this way have not been described. This may be possible due to the rarity of the Bombay phenotype but also because of the IgM produced by the immune system of the mother. Since IgMs are not transported across the microscopic placental

blood vessels (like IgG are) they cannot reach the blood stream of the fetus to provoke the expected acute hemolytic reaction. In popular culture In the July 15, 1952 episode of the popular radio drama *The Lineup*, the plot hinged on identifying a suspect with the rare blood type H, found on the clothes of the victim. In the cooking manga *Yakitate!! Japan*, the King of Monaco was revealed to have Bombay blood, as was Pierrot Bonnaz, who was found out to be the long-lost prince. On the daytime soap opera *General Hospital*, it was believed that Monica's husband Alan could not have been the father of her child, as Alan's blood was AB, Monica's was A, and the child's was thought to be O. However, it was eventually revealed that Alan was indeed the father; he and Monica were both carriers of the h allele and the baby had the Bombay phenotype. The 2003 Anime series *GetBackers* episode 35, the object to be retrieved was a quantity of Bombay blood to save a girl's life. The 2007 Telugu film *Okkadunnadu* revolves around the Bombay Blood Group; the antagonist is in dire need of blood of this blood group, which can only be given by the protagonist. In the 2012 Japanese television drama *Seinaru Kaibutsutachi*, Mie Arima, who has Bombay blood, is killed by the chief nurse Yuka Kasugai with an O+ blood transfusion while undergoing a Caesarean section. In the 2011 Canadian TV series *My Babysitter's a Vampire*, Ethan, one of the main characters, is said to have H-deficient blood, which the vampires of the story consider a delicacy. In the 2012 film *Get the Gringo* the villain (Javi Huerta) has hh blood. Prior to the start of the film, he uses a man, whom also has hh blood, as his personal organ donor. He later attempts to do the same with the man's son. In the 2012 Hindi film *Kahaani* the main antagonist (Milan Damji) has hh blood. In the manga and anime *Kindaichi Case Files*, the case titled *Legend of the Vampire* had several characters with this blood type. The *Stone Cold Steve Austin/Dolph Lundgren* film *The Package* revolves around hh blood. Austin's character is hired by Lundgren's to bring him a mysterious pack, which turns out to be a dose of hh blood. In the 2013 Tamil film *Idharkuthane Aasaipattai Balakumara* the blood group plays an important role in saving the life of a pregnant woman. Only Vijay Sethupathy has that blood group in that movie that makes the plot more interesting. The 2013 film *Radhana Ganda* was based on the Bombay blood group. In an episode of the BBC drama serial *Holby City*, broadcast June 16, 2015, two patients with Bombay blood group, a Mr Qureshi and his daughter Hayley, required surgery which it was thought only one could have, as there was only enough blood for one. In the event, both were saved. In an episode *Dahej Ka Chakravayuh* of Indian crime series *C.I.D.*, Vishakha is about to get married with Abhay but her to be father-in-law demands a kidney from her father in exchange of the wedding because Mr. Uday has a rare blood group named Bombay Blood Group. In a Hindi TV show called *Udaan*, where the main character has the rare Bombay blood group and is hunted for it. In the 2015 episode of CBS's *NCIS: New Orleans* Season 2 Episode 07, a Crypto Analyst working for DARPA who reveals himself having the rare Hh blood group was in need of a new heart transplant which was compromised during transport by an assailant shooting the heart with a gun killing it before it could be transplanted. NCIS gets involved when 2 Navy Paramedics were killed during a house call and one of the Medics security cards was missing leading the story into a balancing of finding a killer and trying to save the life of the Analyst. An episode of the Canadian TV series *Psi Factor: Chronicles of the Paranormal* had the O.S.I.R. team encounter a young

woman with Bombay blood while working to solve the case of a haunting in the underground maintenance tunnels of a major city. In the TV series Stan Lee's Lucky Man (2016) (season 1 episode 6), a plotline revolves around an antagonist with the blood type in need of a kidney transplant, who had a man with the blood type killed for his kidney. In the visual novel Kara no Shōjo, the main character Toko Kuchiki has the Bombay phenotype. In the visual novel 428: Shibuya Scramble, one of the playable characters has a sister who is in need of a heart transplant, but cannot find a donor due to being one of the very few people in Japan with Bombay blood. In the 2017 Tamil film yaakkai romantic crime thriller involving medical scam, the female protagonist (kavitha) has hh blood. In the 2011 Japanese medical drama Doctors: the Ultimate Surgeon season 2 episode 8, Dr Sagara and his team has to perform an esophagus cancer surgery on a patient that has anemia, but the problem is that he had the Bombay blood type. So the team had to perform a non-blood surgery which at the end is a big success. In 2017 Malayalam movie Sathya deals with Bombay blood group as the hero wants Bombay blood to save his girl friend. In 2018 Series 2 of The Good Karma Hospital has an episode dealing with a patient with the rare hh blood type. In the 1989 OAV Vampire Princess Miyu, it's implied that a Kyoto little girl who's seemingly possessed by a Shinma and her parents have Bombay Blood, but not officially confirmed. In the backstory they get into an accident and no one can find donors with the appropriate blood on time; the parents, whose injuries are fatal, beg their treating doctor to donate their blood to their daughter, and this saves the girl's life but kills the parents. In the 2019 Tamil film Pottu, a horror film involving medical scam, a tribal village has many people with the Bombay blood group. 2019 Wild Bill episode 3 (ITV drama, UK) key character has HH blood type and needs to find her father in order to receive a transplant. References External links Hh at BGMUT Blood Group Antigen Gene Mutation Database at NCBI, NIH RMIT University The Bombay, para-Bombay and other H deficiencies BombayBloodGroup.Org an initiative to connect individuals who donate and who are in need of Bombay blood group. Genetics of the Bombay Phenotype Bombay Blood Group