

Cancer Association of South Africa (CANSA)



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Fact Sheet on Childhood Hepatoblastoma

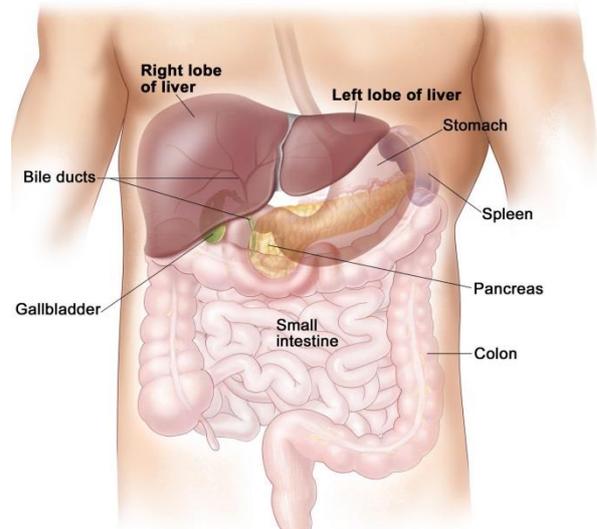
Introduction

The liver is the largest glandular organ in the body and performs many vital functions to keep the body pure of toxins and harmful substances.

It is a vital organ that supports nearly every organ in the body in some facet. Without a healthy liver, a person cannot survive.

[Picture Credit: Liver]

An average adult liver weighs about 1,5kg. Located in the upper-right portion of the abdominal cavity under the diaphragm, the liver consists of four lobes. As far as its blood supply is concerned, it consists of eight (8) segments. It receives about 1.4 litres of blood every minute via the hepatic artery and portal vein.



The liver is considered a gland - an organ that secretes chemicals - because it produces bile, a substance needed to digest fats. Bile salts break up fat into smaller pieces so it can be absorbed more easily in the small intestine.

In addition to producing bile, the liver:

- Detoxifies the blood to rid it of harmful substances such as alcohol and drugs
- Stores some vitamins and iron
- Stores the simple sugar glucose
- Converts stored sugar to usable sugar when the body's sugar (glucose) levels fall below normal.
- Breaks down haemoglobin as well as insulin and other hormones
- Converts ammonia to urea, which is vital in metabolism
- Destroys old red blood cells

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Dip Audiometry and Noise Measurement; Diagnostic Radiographer; Medical Ethicist]

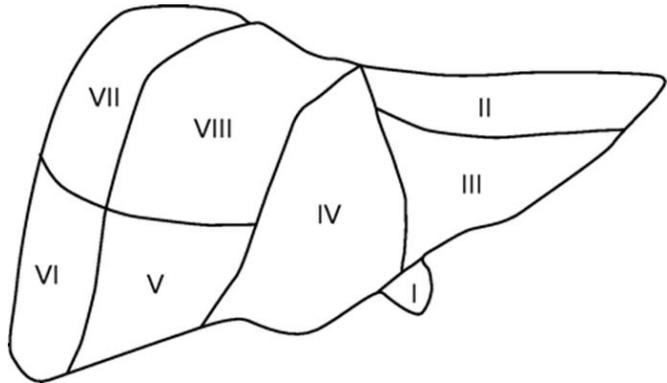
Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

February 2021

The destruction of old red blood cells produces waste that gives faecal matter its usual brown colour. Discolouration of stool - or darkened urine - could signal something is wrong with the liver.

[Picture Credit: Liver Segments]

Another common sign of liver problems is jaundice, the yellowing of the skin and eyes due to the build-up of bilirubin, a waste product of normal haemoglobin breakdown.



Because the liver performs so many vital functions, it is prone to disease.

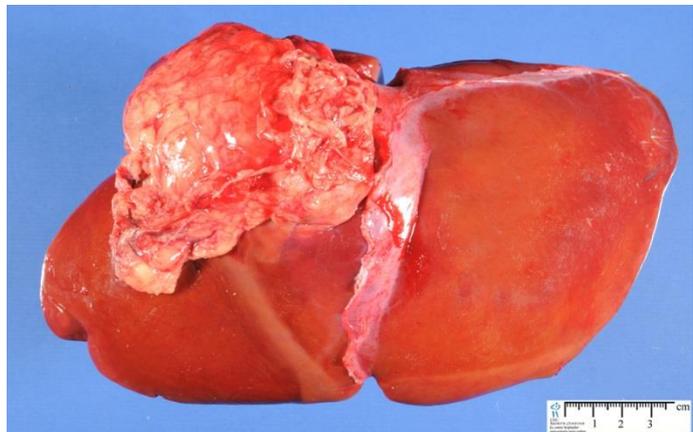
Musick, S.R., Smith, M., Rouster, A.S. & Babiker, H.M. 2020.

“Hepatoblastomas are the most common primary malignant liver tumor in pediatric patients, occurring mostly within the first 2 years of life. The histologic types are subdivided into 2 broad categories: epithelial type and mixed type. Over the last 3 decades, the treatment has advanced with neo-adjuvant chemotherapy now the standard of care for most cases. Neo-adjuvant chemotherapy and surgical resection produce a cure rate of approximately 70%, a vast improvement over the dismal 30% cure rate in the 1970s. Prognosis is based on many factors including alpha-fetoprotein levels, age at the time of diagnosis, completeness of resection, and clinical stage of the disease.”

Hepatoblastoma

Hepatoblastoma is the most common primary liver tumour in children, accounting for just over 1% of paediatric cancers. The aetiology (cause) is unknown, but it has been associated with Beckwith-Weidemann syndrome, familial adenomatous polyposis, and low birth weight. The primary treatment is surgical resection, however, chemotherapy plays an important role by increasing the number of tumours that are resectable. The prognosis for patients with resectable tumours is fairly good, however, the outcome for those with non-resectable or recurrent disease is poor.

[Picture Credit: Epithelial Hepatoblastoma]



Ranganathan, S., Lopez-Terrada, D. & Alaggio, R. 2020.

“Hepatoblastomas (HBs) and pediatric hepatocellular carcinomas (HCCs) together account for almost 80% of primary malignant liver tumors in children and adolescents/young adults. Children's Hepatic International Collaboration (CHIC), Children's Oncology Group (COG), Société Internationale d'Oncologie Pédiatrique (SIOP), and International Childhood Liver Tumors Strategy Group trials have

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contributed to define prognostic factors and risk stratification in these tumors. The recently proposed histologic International Consensus classification of HB and HCC in children based on retrospective analysis from CHIC cases represents the base to define entities with homogeneous clinicopathologic and molecular features. This review will provide a morphologic guide for the upcoming International Liver Tumor treatment trial (Pediatric Hepatic International Tumour Trial) to be conducted through several continents. There will be an emphasis on molecular features and immunohistochemical markers for the definition of the individual histologic subtypes of HB and to better characterize the group of liver tumors in the provisional category of hepatocellular neoplasm-not otherwise specified. A brief overview of HCC in children will also be provided.”

Musick, S.R., Smith, M., Rouster, A.S. & Babiker, H.M. 2020.

“Hepatoblastomas are the most common primary malignant liver tumor in pediatric patients, occurring mostly within the first 2 years of life. The histologic types are subdivided into 2 broad categories: epithelial type and mixed type. Over the last 3 decades, the treatment has advanced with neo-adjuvant chemotherapy now the standard of care for most cases. Neo-adjuvant chemotherapy and surgical resection produce a cure rate of approximately 70%, a vast improvement over the dismal 30% cure rate in the 1970s. Prognosis is based on many factors including alpha-fetoprotein levels, age at the time of diagnosis, completeness of resection, and clinical stage of the disease.”

Incidence of Hepatoblastoma in South Africa.

The National Cancer Registry (2017) does not provide any statistics on the incidence of Hepatoblastoma in South Africa.

Causes of Hepatoblastoma

Although the exact cause of liver cancer is unknown, there are a number of genetic conditions that are associated with an increased risk for developing hepatoblastoma, including the following:

- Beckwith-Wiedemann Syndrome - a congenital (present from birth) growth disorder that causes large body size, large organs, and other symptoms.
- Hemihypertrophy - a rare disorder in which one side of the body grows more than other, causing asymmetry.
- Familial Adenomatous Polyposis - an inherited condition in which numerous adenomatous polyps form mainly in the epithelium of the large intestine.
- Tyrosinaemia - an error of metabolism, usually inborn, in which the body cannot effectively break down the amino acid tyrosine. Symptoms include liver and kidney disturbances and mental retardation. Untreated, tyrosinaemia can be fatal.
- Glycogen Storage Disease Type I - or von Gierke's disease, is the most common of the glycogen storage diseases. This genetic disease results from deficiency of the enzyme glucose-6-phosphatase.
- Galactosaemia - a rare genetic metabolic disorder that affects an individual's ability to metabolise the sugar galactose properly.
- Alpha-1 -Antitrypsin Deficiency – a genetic disorder that causes defective production of alpha 1-antitrypsin (A1AT), leading to decreased A1AT activity in the blood and lungs, and deposition of excessive abnormal A1AT protein in liver cells.

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Children who have a hepatitis B infection at an early age, or those who have biliary atresia (a blockage in the tubes that carry bile), are also at increased risk for developing hepatoblastoma.

Signs and Symptoms of Hepatoblastoma

Symptoms are more common after the tumour becomes large and may include:

- A painless lump in the abdomen
- Swelling or pain in the abdomen
- Weight loss for no known reason
- Loss of appetite
- Early puberty in boys
- Nausea and vomiting
- Jaundice (yellowing of the eyes and skin)
- Fever
- Itching skin
- Enlarged veins on the belly that can be seen through the skin

Diagnosis of Hepatoblastoma

If the doctor suspects liver cancer is causing the child's symptoms, the following tests and procedures may be used to make a final diagnosis:

- Blood tests – a blood sample taken from the child will allow doctors to run tests on the blood including a serum tumour marker test, a complete blood count (CBC) and liver function test - tests that can measure how well the child's liver is functioning, or find substances in the blood that signal liver cancer may be present. Most hepatoblastomas and some hepatocellular carcinomas produce a chemical called alpha-fetoprotein (AFP), which is released into the bloodstream. By measuring levels of AFP in the child's blood, doctors can sometimes tell whether the cancer is responding to treatment
- Abdominal X-Ray – an X-Ray of the organs in the abdomen
- Ultrasound examination – high energy sound waves (ultrasound) are bounced off internal tissues or organs and make echoes in this procedure. The echoes form a picture of body tissues called a sonogram. The picture can be printed to be looked at later.
- CT Scan (computerised tomography) – in this procedure, detailed pictures of the chest and abdomen are taken from different angles by a computer linked to an X-Ray machine. Dye may be injected into a vein or swallowed to help the organs or tissues show up more clearly in the image
- MRI (magnetic resonance imaging) – for this imaging procedure, magnet, radio-waves, and a computer make a series of detailed pictures of areas inside the body

- Biopsy – a sample of the patient’s liver tissue is removed and checked for signs of cancer under a microscope. The sample may be taken during surgery to remove or view the tumour

Subramanian, K.S., Chikhale, M., Barwad, A., Gochhajt, D., Toi, P.C. & Siddaraju, N. 2019.

Hepatoblastoma (HB) constitutes less than 1% of all pediatric malignancies and is the most common malignant tumor of liver in children. The fine-needle aspiration cytological (FNAC) diagnosis and sub-typing of this tumor is challenging, which is of critical importance from its treatment point of view. All cases with a clinicroadiological impression of "HB" during the study period of 1 year were subjected to ultrasound-guided (USG) FNAC and cell blocks were prepared in all cases. Detailed cytopathological examination was carried out based on the cytomorphological pattern and the cell blocks were used to correlate the findings and the final diagnoses were confirmed with the histopathological findings. Four cases were included during this study period. All were children, whose age ranged from 3 months to 10 years. All of them presented with mass per abdomen and increased serum alfa-feto protein (AFP) levels. On a detailed cytological examination, the clinical impression of HB was confirmed in all four cases with a subsequent histological correlation. Based on their distinct cytomorphological pattern, three of them were accurately sub-typed as "fetal type," while the fourth was an "embryonal type of HB." All four cases had the evidence of extramedullary hematopoiesis. We conclude that a precise preoperative FNAC diagnosis with accurate sub-typing of HB is possible purely on cytomorphologic basis which has prognostic and therapeutic implications. Cell blocks are of great use for ancillary studies. Extramedullary hematopoiesis serves as an important "clue" in diagnosis.

- Angiograms – X-rays of blood vessels
- Laparoscopy - doctors make a tiny incision in the abdomen and insert a thin, lighted tube to look at the liver

Weldon, C.B., Madenci, A.L., Tiao, G.M., Dunn, S.P., Langham, M.R., McGahren, E.D., Ranganathan, S., López-Terrada, D.H., Finegold, M.J., Malogolowkin, M.H., Piao, J., Huang, L., Krailo, M.D., Meyers, R.L. & Katzenstein, H.M. 2019.

BACKGROUND: The histopathological assessment of pediatric liver tumors at presentation is critical to establish a diagnosis, guide treatment, and collect appropriate research samples. The purpose of this study was to evaluate complications associated with different approaches to liver biopsy for newly diagnosed hepatoblastoma.

METHODS: Children with hepatoblastoma were enrolled on Children's Oncology Group study AHEP0731 (September 2009-March 2012). This analysis evaluated the study cohort of initially unresectable patients who therefore underwent a biopsy procedure at diagnosis. The primary endpoint was clinically significant postbiopsy hemorrhage, defined as requiring red blood cell transfusion.

RESULTS: We identified 121 children who underwent open (n = 76, 63%), laparoscopic (n = 17, 14%), or percutaneous (n = 28, 23%) liver biopsies. All biopsy procedures yielded adequate tissue for diagnosis. Postbiopsy hemorrhage requiring transfusion occurred after 26% (n = 31) of biopsies. Need for blood product transfusion most frequently occurred following open (n = 27/76, 36%) and laparoscopic (n = 4/17, 24%) biopsies, compared with percutaneous (n = 0/28, 0%) biopsies (p < 0.01).

CONCLUSIONS: Pretreatment biopsy of pediatric liver tumors via a percutaneous approach yielded the lowest frequency of clinically significant hemorrhage requiring transfusion, without evidence of sacrificing diagnostic accuracy.

Staging of Hepatoblastoma

Once liver cancer is found, more tests will be done to find out if cancer cells have spread to other parts of the body. Doctors call this process 'staging' because they need to find out what stage the cancer is in. Once they have that information, the doctors can plan the best treatment for the child.

Hepatoblastoma is staged as follows:

Stage I

Tumour is completely resectable via wedge resection or lobectomy; tumour has pure foetal histologic (PFH) results; AFP level is within reference range within 4 weeks of surgery

Stage IIA

Tumour is completely resectable; tumour has histologic results other than PFH (unfavorable histology [UH])

Stage IIB

Tumour is completely resectable; AFP findings are negative at time of diagnosis (i.e., no marker to follow)

Stage IIC

Tumour is completely resected or is rendered completely resectable by initial radiotherapy or chemotherapy or microscopic residual disease is present; AFP level is elevated 4 weeks after resection

Stage III

(Any of the following): Either the tumour is initially unresectable but is confined to 1 lobe of the liver, gross residual disease is present after surgery, the tumour ruptures or spills preoperatively or intraoperatively, or regional lymph nodes are involved

Stage IV

Distant bone or lung metastasis has occurred

Treatment of Hepatoblastoma

There are a number of treatments for liver tumours. Hepatoblastoma and hepatocellular carcinoma are treated in different ways. Although both tumours require complete surgical removal for treatment to be successful, they respond differently to chemotherapy. Hepatoblastoma responds well to chemotherapy while hepatocellular carcinoma tumours are usually treated with surgery alone.

Surgery - surgical removal of the tumour is the most important component of successful treatment for liver tumours. An operation is performed to remove the tumour and the part of the liver where the cancer cells are found. If the cancer cells have spread to other parts of the body, surgery may also remove the tumours from these areas. The most common places for liver cancer to spread include tissues that surround the liver, the lungs or the brain.

Chemotherapy - chemotherapy is the use of drugs to destroy cancer cells. Chemotherapy may be used before surgery to shrink the tumour so that it can be surgically removed, or it can be used after

surgery to destroy any remaining cancer cells. While hepatoblastoma usually responds very well to chemotherapy, hepatocellular carcinoma is very resistant to chemotherapy. Different combinations of cisplatin, vincristine, 5-fluorouracil and doxorubicin are used.

Chemoembolisation - sometimes, when systemic (through the blood stream) chemotherapy does not work, chemoembolization is used as a treatment. This means that the chemotherapy medications are placed directly into the tumour. In the case of liver cancer, the main artery that delivers blood to the liver is injected with chemotherapy drugs and embolising substances (treatments that block or slow the flow of blood to the tumour). This prevents nutrients from feeding the tumour and gives the chemotherapy drugs more time to destroy the cancer cells.

Liver transplantation - if the tumour has spread throughout the liver, or it is not possible to preserve enough normal liver when surgically removing the tumour, the liver may be replaced entirely with a portion of healthy liver. Patients who have a liver transplant need to take medications to suppress the immune system for the rest of their lives.

Sindhi, R., Rohan, V., Bukowinski, A., Tadros, S., de Ville de Goyet, J., Rapkin, L. & Ranganathan, S. 2020.

“Unresectable hepatocellular carcinoma (HCC) was first removed successfully with total hepatectomy and liver transplantation (LT) in a child over five decades ago. Since then, children with unresectable liver cancer have benefitted greatly from LT and a confluence of several equally important endeavors. Regional and trans-continental collaborations have accelerated the development and standardization of chemotherapy regimens, which provide disease control to enable LT, and also serve as a test of unresectability. In the process, tumor histology, imaging protocols, and tumor staging have also matured to better assess response and LT candidacy. Significant trends include a steady increase in the incidence of and use of LT for hepatoblastoma, and a significant improvement in survival after LT for HCC with each decade. Although LT is curative for most unresectable primary liver sarcomas, such as embryonal sarcoma, the malignant rhabdoid tumor appears relapse-prone despite chemotherapy and LT. Pediatric liver tumors remain rare, and diagnostic uncertainty in some settings can potentially delay treatment or lead to the selection of less effective chemotherapy. We review the current knowledge relevant to diagnosis, LT candidacy, and post-transplant outcomes for these tumors, emphasizing recent observations made from large registries or larger series.”

Herden, U., Grabhorn, E., Lenhartz, H., Kütemeier, R., Fischer, L. 2019.

BACKGROUND: Hepatoblastoma is a rare malignancy but the most common primary hepatic malignancy in childhood. Pediatric liver transplantation (LT) offers the possibility to achieve a complete resection in otherwise unresectable tumors. Almost no data are available regarding specific surgical technique of LT in children with hepatoblastoma.

METHODS: We analyzed all children with hepatoblastoma and LT between 2007 and 2012. Special regard was given to the surgical technique and long-term follow-up.

RESULTS: Overall 7 children were transplanted with the diagnosis of hepatoblastoma (5 male, 2 female). Thereof, 4 children (median age was 11 months, range, 6-31 months) underwent "primary" LT for hepatoblastoma Pretreatment Extent of Disease III to IV. A 4-year-old boy received "salvage" LT for recurrent hepatoblastoma 2.5 years after successful liver resection. Another 15-year-old boy was transplanted as a prophylactic treatment after repeated liver resection for hepatoblastoma due to the high recurrence risk. A 14-year-old boy underwent LT due to complications following liver resection for hepatoblastoma during infancy. In all children, extensive en bloc hepatectomy was

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performed together with resection of the adjoining retroperitoneal tissue and regional lymphadenectomy. Actually, all children are alive without tumor recurrence median 7.1 years after LT (range, 5.7-10.7 years).

CONCLUSION: Our data show an excellent long-term outcome in selected children with hepatoblastoma undergoing standardized en bloc hepatectomy for "primary" and "rescue" LT with 100% overall and recurrence-free survival.

de Freitas Paganoti, G., Tannuri, A.C.A., Dantas Marques, A.C., Torres, R.R., Mendes Gibelli, N.E. & Tannuri. U. 2019.

BACKGROUND: Surgery is a key factor in the treatment of hepatoblastoma, but choosing between an aggressive resection and liver transplant may be an extremely difficult task. The aim of this study was to describe the outcomes of patients with advanced hepatoblastoma: pretreatment extent of disease (PRETEXT)/post-treatment extent of disease (POST-TEXT) III and IV undergoing aggressive resections or living donor liver transplant in cases involving the entire liver. Based on this experience, a new protocol for the treatment of these patients was proposed.

METHODS: A retrospective study included patients with advanced hepatoblastoma (POST-TEXT III and IV) who were referred for a liver transplant from 2010 to 2017.

RESULTS: A total of 24 children were included: 13 (54.2%) were male, with a median age at diagnosis of 42 months (range, 15-120 months), and a history of prematurity was identified in 20.8% of the patients. Ten cases (41.7%) were staged as PRETEXT/POST-TEXT III, and 12 cases (50.0%) were staged as PRETEXT/POST-TEXT IV. Two patients were referred after posthepatectomy recurrence. Five patients underwent a liver transplant, with recurrence and death in 2 patients (40.0%) within a mean period of 6 months. In the extensive hepatectomy group, there was recurrence in 6 patients (31.6%), with disease-free outcomes and overall survival in 63.2% and 94.7% of patients, respectively.

CONCLUSION: In cases of advanced hepatoblastoma, an extensive surgical approach is a valuable option. The fact that the team was fully prepared to proceed with living donor liver transplant allowed the surgeon to be more aggressive and to switch to transplantation when resection was not possible.

Carrillo-Reixach, J., Torrens, L., Simon-Coma, M., Royo, L., Domingo-Sàbat, M., Abril-Fornaguera, J., Akers, N., Sala, M., Ragull, S., Arnal, M., Villalmanzo, N., Cairo, S., Villanueva, A., Kappler, R., Garrido, M., Guerra, L., Sábado, C., Guillén, G., Mallo, M., Piñeyro, D., Vázquez-Vitali, M., Kuchuk, O., Mateos, M.E., Ramírez, G., Santamaría, M.L., Mozo, Y., Soriano, A., Grotzer, M., Branchereau, S., de Andoin, N.G., López-Ibor, B., López-Almaraz, R., Salinas, J.A., Torres, B., Hernández, F., Uriz, J.J., Fabre, M., Blanco, J., Paris, C., Bajčiová, V., Laureys, G., Masnou, H., Clos, A., Belendez, C., Guettier, C., Sumoy, L., Planas, R., Jordà, M., Nonell, L., Czauderna, P., Morland, B., Sia, D., Losic, B., Buendia, M.A., Sarrias, M.R., Llovet, J.M. & Armengol, C. 2020.

Background & aims: Hepatoblastoma (HB) is a rare disease. Nevertheless, it is the predominant pediatric liver cancer, with limited therapeutic options for patients with aggressive tumors. Herein, we aimed to uncover the mechanisms of HB pathobiology and to identify new biomarkers and therapeutic targets in a move towards precision medicine for patients with advanced HB.

Methods: We performed a comprehensive genomic, transcriptomic and epigenomic characterization of 159 clinically annotated samples from 113 patients with HB, using high-throughput technologies.

Results: We discovered a widespread epigenetic footprint of HB that includes hyperediting of the tumor suppressor BLCAP concomitant with a genome-wide dysregulation of RNA editing and the overexpression of mainly non-coding genes of the oncogenic 14q32 DLK1-DIO3 locus. By unsupervised analysis, we identified 2 epigenomic clusters (Epi-CA, Epi-CB) with distinct degrees of DNA hypomethylation and CpG island hypermethylation that are associated with the C1/C2/C2B transcriptomic subtypes. Based on these findings, we defined the first molecular risk stratification of HB (MRS-HB), which encompasses 3 main prognostic categories and improves the current clinical risk

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stratification approach. The MRS-3 category (28%), defined by strong 14q32 locus expression and Epi-CB methylation features, was characterized by CTNNB1 and NFE2L2 mutations, a progenitor-like phenotype and clinical aggressiveness. Finally, we identified choline kinase alpha as a promising therapeutic target for intermediate and high-risk HBs, as its inhibition in HB cell lines and patient-derived xenografts strongly abrogated tumor growth.

Conclusions: These findings provide a detailed insight into the molecular features of HB and could be used to improve current clinical stratification approaches and to develop treatments for patients with HB.

Lay summary: Hepatoblastoma is a rare childhood liver cancer that has been understudied. We have used cutting-edge technologies to expand our molecular knowledge of this cancer. Our biological findings can be used to improve clinical management and pave the way for the development of novel therapies for this cancer.

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The [South African National Clinical Trials Register](#) provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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Sources and References Consulted or Utilised

Busweiler, L.A., Wilnen, M.H., Wilde, J.C., Sieders, E., Terwisscha van Scheltinga, S.E., van Heum, L.W. Ziros, J., Bakx, R. & Hejl, H.A. 2017. Surgical treatment of childhood hepatoblastoma in the Netherlands (2990-2013). *Pediatr Surg Int.* 2017 Jan;33(1):23-31. doi: 10.1007/s00383-016-3989-8. Epub 2016 Oct 11.

Carrillo-Reixach, J., Torrens, L., Simon-Coma, M., Royo, L., Domingo-Sàbat, M., Abril-Fornaguera, J., Akers, N., Sala, M., Ragull, S., Arnal, M., Villalmanzo, N., Cairo, S., Villanueva, A., Kappler, R., Garrido, M., Guerra, L., Sábado, C., Guillén, G., Mallo, M., Piñeyro, D., Vázquez-Vitali, M., Kuchuk, O., Mateos, M.E., Ramírez, G., Santamaría, M.L., Mozo, Y., Soriano, A., Grotzer, M., Branchereau, S., de Andoin, N.G., López-Ibor, B., López-Almaraz, R., Salinas, J.A., Torres, B., Hernández, F., Uriz, J.J., Fabre, M., Blanco, J., Paris, C., Bajčiová, V., Laureys, G., Masnou, H., Clos, A., Belendez, C., Guettier, C., Sumoy, L., Planas, R., Jordà, M., Nonell, L., Czauderna, P., Morland, B., Sia, D., Losic, B., Buendia, M.A., Sarrias, M.R., Llovet, J.M. & Armengol, C. 2020. Epigenetic footprint enables molecular risk stratification of hepatoblastoma with clinical implications. *J Hepatol.* 2020 Aug;73(2):328-341.

Children's Cancer Research Fund

http://www.childrenscancer.org/main/liver_cancer_hepatoblastoma/

Children's Hospital of Pittsburgh

<http://www.chp.edu/CHP/hepatoblastoma>

Children's Oncology Group

<http://www.childrensoncologygroup.org/index.php/hepatoblastomaandhepatocellularcarcinoma?id=190>

de Freitas Paganoti, G., Tannuri, A.C.A., Dantas Marques, A.C., Torres, R.R., Mendes Gibelli, N.E. & Tannuri, U. 2019. Extensive hepatectomy as an alternative to liver transplant in advanced hepatoblastoma: a new protocol used in a pediatric liver transplantation center. *Transplant Proc.* 2019 Jun;51(5):1605-1610. doi: 10.1016/j.transproceed.2019.03.004.

Healthline

<http://www.healthline.com/human-body-maps/liver>

Dana-Farber Cancer Institute

<http://www.dana-farber.org/Health-Library/Childhood-Hepatoblastoma.aspx>

Epithelial Hepatoblastoma

https://www.google.co.za/search?q=hepatoblastoma&source=lnms&tbm=isch&sa=X&ei=T-3YU9rHMIXe7Abms4GIBA&sqi=2&ved=0CAYQ_AUoAQ&biw=1517&bih=714&dpr=0.9#facrc=_&imgdii=_&imgrc=cUJcaMdOnzp0XM%253A%3BbjAVFJfYUc-8MM%3Bhttp%253A%252F%252Fwww.humph.com%252FIMG%252Fjpg_14228_hepatoblastoma_0808_01.jpg%3Bhttp%253A%252F%252Fwww.humph.com%252Fspip.php%253Farticle14228%3B1000%3B633

Herden, U., Grabhorn, E., Lenhart, H., Kütemeier, R., Fischer, L. 2019. Excellent outcome following liver transplantation for hepatoblastoma using an extensive en bloc hepatectomy technique. *Transplant Proc.* 2019 Jun 28. pii: S0041-1345(18)31056-X. doi: 10.1016/j.transproceed.2019.04.025. [Epub ahead of print]

Liver

https://www.google.co.za/search?q=anatomy+of+liver&source=lnms&tbm=isch&sa=X&ei=KurYU6fKGe_07AabyIDQBw&sqi=2&ved=0CAYQ_AUoAQ&biw=1517&bih=714&dpr=0.9#facrc=_&imgdii=_&imgrc=daTbWji4NXGiNM%253A%3BkPS9vTKdYF1-iM%3Bhttps%253A%252F%252Fherbsforhealthandwellbeing.files.wordpress.com%252F2014%252F01%252Fliver-anatomy.jpg%3Bhttps%253A%252F%252Fherbsforhealthandwellbeing.wordpress.com%252Ftag%252Fanatomy-of-the-liver%252F%3B1600%3B1466

Liver Segments

<http://theoncologist.alphamedpress.org/content/5/6/445/F5.expansion.html>

Medscape

<http://emedicine.medscape.com/article/986802-overview>

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February 2021

Musick, S.R., Smith, M., Rouster, A.S. & Babiker, H.M. 2020. Hepatoblastoma. *In*: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan. 2020 Aug 23.

Namgoong, J.M., Choi, J.U., Hwang, S., Oh, S.H. & Park, G.C. 2019. Pediatric living donor liver transplantation with homograft replacement of retrohepatic inferior vena cava for advanced hepatoblastoma. *Ann Hepatobiliary Pancreat Surg.* 2019 May;23(2):178-182. doi: 10.14701/ahbps.2019.23.2.178. Epub 2019 May 31.

National Cancer Institute

<http://www.cancer.gov/about-cancer/treatment/clinical-trials/what-are-trials>

Ranganathan, S., Lopez-Terrada, D. & Alaggio, R. 2020. Hepatoblastoma and pediatric hepatocellular carcinoma: an update. *Pediatr Dev Pathol.* Mar-Apr 2020;23(2):79-95.

Sharma, D., Subbarao, G. & Sexena, R. 2017. Hepatoblastoma. *Semin Diagn Pathol.* 2017 Mar;34(2):192-200. doi: 10.1053/j.semmp.2016.12.015. Epub 2016 Dec 23.

Sindhi, R., Rohan, V., Bukowinski, A., Tadros, S., de Ville de Goyet, J., Rapkin, L. & Ranganathan, S. 2020. Liver transplantation for pediatric liver cancer. *Cancers (Basel).* 2020 Mar 19;12(3):720.

Stanford Children's Health

<http://www.stanfordchildrens.org/en/topic/default?id=hepatoblastoma-90-P02728>

Subramanian, K.S., Chikhale, M., Barwad, A., Gochhajt, D., Toi, P.C. & Siddaraju, N. 2019. Fine-needle aspiration cytology and cell block in diagnosis and subtyping of hepatoblastoma. *Diagn Cytopathol.* 2019 Jul;47(7):706-710. doi: 10.1002/dc.24167. Epub 2019 Apr 22.

The Oncologist

<http://theoncologist.alphamedpress.org/content/5/6/445.full>

Weldon, C.B., Madenci, A.L., Tiao, G.M., Dunn, S.P., Langham, M.R., McGahren, E.D., Ranganathan, S., López-Terrada, D.H., Finegold, M.J., Malogolowkin, M.H., Piao, J., Huang, L., Krailo, M.D., Meyers, R.L. & Katzenstein, H.M. 2019. Evaluation of the diagnostic biopsy approach for children with hepatoblastoma: a report from the Children's Oncology Group AHEP 0731 Liver Tumor Committee. *J Pediatr Surg.* 2019 May 11. pii: S0022-3468(19)30347-1. doi: 10.1016/j.jpedsurg.2019.05.004. [Epub ahead of print]