Republic of Iraq Ministry of Higher Education and Scientific Research University of Babylon/College of pharmacy

**Determination of liver function test in DM patients** 

Submitted to the council of college of pharmacy-Babylon Univesity As partial of the requirement for BSc degree of pharmacy

BY

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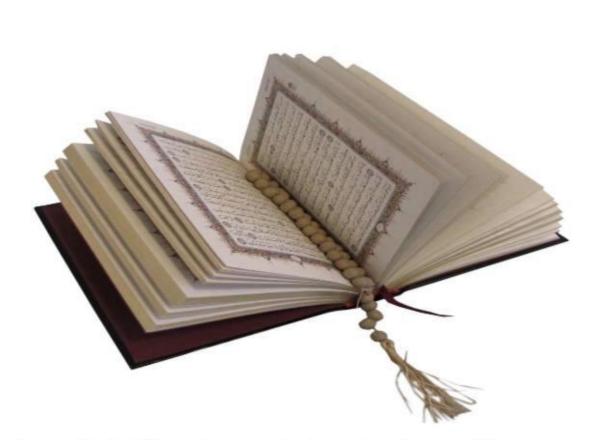
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2024



[اقْرَأْ بِاسْمِ رَبِّكَ الَّذِي خَلَقَ (1) خَلَقَ الْإِنْسَانَ مِنْ عَلَقٍ (2) اقْرَأْ وَرَبُّكَ الْأَكْرَمُ (3) الَّذِي عَلَّمَ بِالْقَلَمِ (4) عَلَّمَ الْإِنْسَانَ مَا لَمْ يَعْلَمُ (5)]

صدق الله العظيم سورة العلق الأية(1-5) بسم الخالق اهدي تعب عمري وسنيني لمن تجعدت يديه ساعياً لرعايتي، لمن شاب شعر ها حرصاً عليّ، للحظات الخوف التي صنعتني، للكسور التي حاولت تحطيم قدمي مانعة أياي من اكمال الطريق،الطريق نحو القمة لأيام البرد القارص وأصابعي المتجمدة وبالكاد استطيع الأمساك بقلمي، ي...وأيام الحر والعرق المتصبب من جبيني بهذه الكلمات توج النجاح وانتهت الرحلة وحصدت نتيجة الصمود

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## Abstract

Blood samples were collected from Marjan Hospital and Imam Sadiq Hospital, the main laboratory, Clinical Chemistry Division, and others from the consulting laboratory and the emergency laboratory for the period from 11/2/2023 until 30/3/2024. We conducted tests using an advanced device for chemical analysis. The tests included the following (fasting blood sugar test, blood test Urea, creatine test, in addition to liver function test )for research and investigation regarding our important topic for human life, which is Determination of liver function test in DM patients

## Chapter one

## Introduction

Diabetes mellitus (DM), commonly known as just diabetes, is a group of metabolic disorders characterized by a high blood sugar level over a prolonged period of time.

Classic signs and symptoms of DM include polydipsia (excessive thirst), polyuria (excessive urination), and polyphagia (excessive hunger). Individuals with type 1 DM may additionally present with unintentional weight loss.

If left untreated, diabetes can cause many health complications:

Acute complications can include diabetic ketoacidosis, hyperosmolar hyperglycemic state, or death.

Serious long-term complications include cardiovascular disease, stroke, chronic kidney disease, foot ulcers, damage to the nerves, damage to the eyes and cognitive impairment..[2][5]

Diabetes is due to either the pancreas not producing enough insulin, or the cells of the body not responding properly to the insulin produced [12]. There are three main types of diabetes mellitus[2]

\_Type 1 diabetes results from failure of the pancreas to produce enough insulin due to loss of beta cells.[12].This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes".The loss of beta cells is caused by an autoimmune \_mediated destruction. [2]

\_Type 2 diabetes begins with insulin resistance, a condition in which cells fail to respond to insulin properly. As the disease progresses, a lack of insulin may also develop. This form was previously referred to as "non insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes"[2]. \_Gestational diabetes is the third main form, and occurs when pregnant women without a previous history of diabetes develop high blood sugar levels[2].

Type 1 diabetes must be managed with insulin injections.`

Prevention and treatment of type 2 diabetes involves maintaining a healthy diet [15], regular physical exercise, a normal body weight, and avoiding use of tobacco.[18].

Control of blood pressure and maintaining proper foot and eye care are important for people with the disease[10].

Insulin and some oral medications can cause low blood sugar.

Weight loss surgery in those with obesity is sometimes an effective measure in those with type 2 diabetes[19].

Gestational diabetes usually resolves after the birth of the baby.

Rates are similar in women and men. Trends suggest that rates will continue to rise[22] [23].

Diabetes at least doubles a person's risk of early death [23].

## **Effects of Diabetes on Liver Health**

Diabetes can have significant consequences on the liver, both directly and indirectly. The liver plays a critical role in regulating blood sugar levels and metabolizing various nutrients. Here are some of the consequences of diabetes on liver health:

1\_Non-Alcoholic Fatty Liver Disease (NAFLD)

NAFLD is a common liver condition that is closely associated with diabetes. It occurs when excess fat accumulates in the liver cells, leading to inflammation and potential liver damage. Insulin resistance, a hallmark of type 2 diabetes, can contribute to the development and progression of NAFLD[24].

Non-Alcoholic Steatohepatitis (NASH)

NASH is a more severe form of NAFLD characterized by liver inflammation and damage. It can lead to fibrosis (scarring) of the liver, cirrhosis, and, in some cases, liver failure. People with diabetes, particularly type 2 diabetes, are at an increased risk of developing NASH[25]..

2\_Impaired Glucose Regulation

The liver plays a crucial role in regulating blood glucose levels. In individuals with diabetes, especially type 2 diabetes, the liver may produce excessive glucose, leading to elevated blood sugar levels. This can contribute to difficulties in glycemic control [26]..

**Increased Risk of Hypoglycemia** 

In people with diabetes who are on certain medications like sulfonylureas, the liver's ability to regulate glucose production can be impaired [27].. This

can result in a higher risk of hypoglycemia (low blood sugar) if these medications are not properly adjusted

#### **3\_Impaired Lipid Metabolism**

Diabetes can affect the way the liver processes lipids (fats), leading to elevated levels of triglycerides and non-high-density lipoprotein (non-HDL) cholesterol. This can contribute to an increased risk of cardiovascular disease[28].

#### **4\_Risk of Cirrhosis and Liver Failure**

Over time, uncontrolled diabetes, especially in combination with other risk factors like obesity and excessive alcohol consumption, can lead to cirrhosis (advanced scarring of the liver) and, in severe cases, liver failure[29].

#### 5\_Risk of Hepatocellular Carcinoma

In individuals with advanced liver disease, such as cirrhosis due to NAFLD or NASH, there is an increased risk of developing hepatocellular carcinoma, which is a type of liver cancer[30]..

It's important for patients with diabetes to manage their insulin resistance and hyperglycemia effectively through lifestyle changes, medication management, and regular medical check-ups. Controlling blood sugar levels, maintaining a healthy weight, and addressing other risk factors like high blood pressure and high cholesterol can help reduce the risk of liver complications associated with diabetes. Consulting with a diabetes specialis is key for managing both diabetes and its potential liver consequences[31].

#### -The effect of diabetes on liver enzymes

The liver has an essential part in the maintenance of glucose homeostasis [1]. A number of markers indicating liver injury, including  $\gamma$ -glutamyl-transferase (GGT), aspartate aminotransferase (AST), Alkaline phosphatase (ALP) and alanine aminotransferase (ALT) are measures for non-alcoholic fatty liver disease (NAFLD) which has been associated with insulin resistance [2] and the risk of diabetes [3].

Diabetes mellitus is one of the key public health problem as well as a leading factor of mortality and morbidity globally [4, 5]. As stated by International Diabetes Federation (IDF), approximately 1 out of 11 adult people in the world would be afflicted with diabetes mellitus [6]. Nearly 80% of diabetic subjects are residents of low and middle-income countries, and countries from South-East Asia especially are influenced by this disease [6]. Diabetes has been related to various liver illnesses such as NAFLD, hepatocellular carcinoma and cirrhosis [3, 7, 8].

These liver diseases are regarded as major contributors to death among diabetic patients [9]. An important marker of liver damage in NAFLD disease is altered liver enzyme levels [10] which are biological markers linking liver disease and diabetes [11]. Specific focus has been made on the contribution of liver enzymes to prediction of diabetes. In this respect, although many studies have shown a relation between diabetes and elevated liver enzymes, the results remain inconsistent [12]. Some studies showed significant relationship between high levels of AST, ALT, GGT and diabetes [13, 14]. In another study, a significant increase was observed for GGT, ALT and ALP levels but not AST [11]. Some studies showed that significant increases in ALT and AST are associated with diabetes [7, 15, 16]. On the other hand, in some studies, only an increase in GGT was associated with diabetes [17]. Considering the high prevalence of diabetes in Iran and its implications on cardiovascular diseases [18], it is of interest to determine the relationship between the levels of liver enzymes and diabetes. Our aim was to investigate the correlation of the level of liver enzymes with diabetes in the adult population of Rafsanjan. Moreover, we evaluated the association between liver enzyme levels within their normal ranges and the odds of diabetes.

## Chapter two

## **Methods**

The previously listed results were examined by a special device called Automated biochemistry analyzer respons®910.

#### **DESCRIPTION**

respons®910 is a bench top analyzer with a throughput of 100 to 150 tests/hour. This analyzer is the ideal system for laboratories with a test volume up to 500 tests per shift.it is a compact and fully-automated bench top analyzer for maximum efficiency. During its development, special attention was paid to easy handling and optimized work flow thus leading to the ideal clinical chemistry system for many laboratories.

CHARACTER Operation	RISTICS
automate	d
Configuration	
compact	
Sample type	
	asma, whole blood, urine
Other measure with imm	d parameters unoturbidimetric analysis
Options	
	ode reader, with STAT port, with crash sensor, with clot detection, connectivity
Throughput	
100 p/h, <sup>2</sup>	150 p/h
Sample volume	
0.05 ml	
(0.00169)	1 US fl oz)
Reagent volum	
Max.: 0.2	5 ml
(0.01 US	fl oz)
Min.: 0.0 <sup>2</sup>	1 ml
(0 US fl o	DZ)

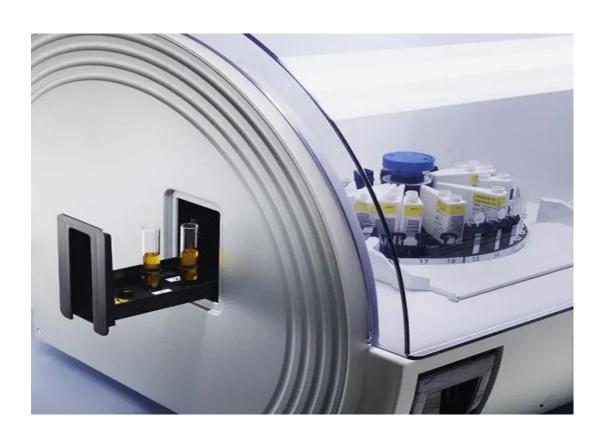
Number of reagent positions

3	0 unit
Weight	
6	i0 kg
(1	132.3 lb)
Length	
6	7 cm
(2	26.4 in)
Width	
6	0 cm
(2	23.6 in)
Height	
6	0 cm
(2	23.6 in)









## Kits for respons



<ul> <li>ALAT (GPT) FS (IFCC mod.)</li> <li>Albumin FS</li> <li>Albumin in Urine/CSF FS (Microalbumin)</li> <li>Alkaline phosphatase FS IFCC 37°C</li> <li>α-Amylase CC FS</li> </ul>	<ul> <li>Antistreptolysin O FS</li> <li>Apolipoprotein A1 FS</li> <li>Apolipoprotein B FS</li> <li>ASAT (GOT) FS (IFCC mod.)</li> </ul>			
<ul> <li>Bicarbonate FS</li> <li>Bilirubin Auto Direct FS</li> </ul>	<ul> <li>Bilirubin Auto Total FS</li> </ul>			
- Calcium P FS	Cleaner respons <sup>®</sup> 920/940/Cleaner A/Cleaner B			
Chimneys	<ul> <li>Complement C3c FS</li> </ul>			
Chloride 21 FS	Complement C4 FS			
<ul> <li>Cholesterol FS</li> <li>Cholinesterase FS</li> </ul>	<ul> <li>Creatinine FS</li> <li>Creatinine PAP FS</li> </ul>			
Chomesterase FS     CK-MB FS	Creatinine FAF FS			
CK-NAC FS	• CRP U-hs			
Cleaner A	Cystatin C FS			
■ Cleaner B				
D-Dimer FS				
Ethanol FS				
- Ferritin SR				
<ul> <li>Gamma-GT FS (Szasz mod./IFCC stand.)</li> <li>Glucose GOD FS</li> </ul>	Glucose Hexokinase FS			
■ oneHbA1c FS	• HDL-C Immuno FS			
- HbA1c net FS	B-Hydroxybutyrate 21 FS			
<ul> <li>HDL-c direct FS</li> </ul>				
Immunoglobulin A ES	. Immunoglobulin M ES			
Immunoglobulin A FS	<ul> <li>Immunoglobulin M FS</li> <li>Iron FS Ferene</li> </ul>			
	- ITOM EN FORONO			
<ul> <li>Immunoglobulin E FS</li> <li>Immunoglobulin G FS</li> </ul>	ISE Urine diluent			

<ul> <li>Lactate FS</li> <li>LDH 21 FS (IFCC mod.)</li> <li>LDL-c direct FS</li> <li>LDL-C Select FS</li> </ul>	<ul> <li>Lipase DC FS</li> <li>Lp(a) 21 FS</li> <li>Lp-PLA<sub>2</sub> FS</li> </ul>
<ul> <li>Magnesium XL FS</li> <li>Myoglobin FS</li> </ul>	
- NEFA FS	
<ul> <li>Pancreatic amylase CC FS</li> <li>Phosphate FS</li> <li>Phospholipids FS</li> </ul>	<ul> <li>Potassium FS</li> <li>Prealbumin FS</li> <li>Procalcitonin FS</li> </ul>
Rheumatoid factor FS	
Rheumatoid factor FS	

- Sodium FS
- Total bile acids 21 FS (serum)
- Total bile acids 21 FS (stool)
- Total protein FS
- UIBC FS
- Urea FS

- Total Protein UC FS
- Transferrin FS
- Triglycerides FS
- Uric acid FS TOOS

# **Chapter three**

### **Result and discussion**

The correlation coefficient is measured on a scale that varies from + 1 through 0 to - 1. Complete correlation between two variables is expressed by either.

	Mean	SD	CORRELATION CREATININE & UREA	CORRELATIO N GOT& GPT	CORRE GOT UREA	CORRE GPT,CRE A	CORRE GPT,URE ATININ	CORRE GOT,R EATINI N
CREATININ mmol/liter	99.7	32.9	0.139	0.14	0.052	0.00012	0.08	0.0005
UREAmmol/ liter	4.96	2.9						
GOT IU/L	26.9	14.5						
GPT IU/L	27.9	19.3						

There is adirect relationship between the studied variable coefficients the excretion of waste products and toxins such as urea, creatinine and uric acid, regulation of extracellular fluid volume, serum osmolality and electrolyte concentrations

Serum creatinine is also utilized in GFR estimating equations such as the Modified Diet in Renal Disease (MDRD) and the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation. These eGFR equations are superior to serum creatinine alone since they include race, age, and gender variables. GFR is classified into the following stages based on kidney disease.

Urea or BUN is a nitrogen-containing compound formed in the liver as the end product of protein metabolism and the urea cycle. About 85% of urea is

eliminated via kidneys; the rest is excreted via the gastrointestinal (GI) tract. Serum urea levels increase in conditions where renal clearance decreases (in acute and chronic renal failure/impairment). Urea may also increase in other conditions not related to renal diseases such as upper GI bleeding, dehydration, catabolic states, and high protein diets. Urea may be decreased in starvation, low-protein diet, and severe liver disease. Serum creatinine is a more accurate assessment of renal function than urea; however, urea is increased earlier in renal disease.

#### Alanine transaminase test

Alanine transaminase (ALT), one of the most important liver function tests, is an enzyme that contributes to the breakdown of proteins, and its elevation indicates liver damage.

#### Aspartate aminotransferase test

Aspartate transaminase (AST) is one of the main enzymes in the liver, and a high AST indicates liver damage or disease.

#### Alkaline phosphatase test

Alkaline Phosphatase (ALP) test is an enzyme found in the liver, bile ducts, and bones, and high levels indicate liver damage or liver disease, bile duct obstruction, or bone disease.

#### Albumin test

Albumin is the main protein made by the liver, and it performs many important functions in the body, such as nourishing tissues, transporting hormones and vitamins in the body, and preventing fluid leakage from blood vessels. A liver function test measures the quality of making this protein, and low levels indicate that the liver is not working properly. good.

### **References**

1. . "Diabetes Blue Circle Symbol" . International Diabetes Federation. 17 March 2006.

2. . "Diabetes Fact sheet  $N^\circ 312"$  . WHO. October 2013. Archived from the original .

3. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN (July 2009). "Hyperglycemic crises in adult patients with diabetes"

4. Krishnasamy S, Abell TL (July 2018). "Diabetic Gastroparesis: Principles and Current Trends in Management" .

5. Saedi, E; Gheini, MR; Faiz, F; Arami, MA (15 September 2016). "Diabetes mellitus and cognitive impairments" . World

6. Chiang JL, Kirkman MS, Laffel LM, Peters AL (July 2014). "Type 1 diabetes through the life span: a position statement of the American Diabetes Association" . Diabetes Care. 37 (7): 2034–54. doi:10.2337/dc14-1140 . PMC 5865481 . PMID 24935775 .

7. Causes of Diabetes" . National Institute of Diabetes and Digestive and Kidney Diseases. June 2014. Archived from the original on 2 February 2016. Retrieved February 2016

 Ripsin, CM; Kang, H; Urban, RJ (January 2009). "Management of blood glucose in type 2 diabetes mellitus" (PDF). American Family Physician. 79 (1): 29-. PMID 19145963 . Archived (PDF)from the original on 2013-05-05. 9. Brutsaert, Erika F. (February 2017). "Drug Treatment of Diabetes Mellitus" . MSDManuals.com. Retrieved 12 October 2018

10. IDFDIABETESATLASNinthEdition2019"(PDF).www.diabetesatlas.org.Retrieved18 May2020

11. About diabetes" . World Health Organization. Archived from the original on 31 March 2014. Retrieved 4 April 2014.

12. 12. Shoback DG, Gardner D, eds. (2011). "Chapter 17". Greenspan's basic
& clinical endocrinology (9th ed.). New York: McGraw-Hill Medical. ISBN 978-0-07-162243-1.

13. . Norman A, Henry H (2015). Hormones. Elsevier. pp. 136–137.ISBN 9780123694447.

14. . RSSDI textbook of diabetes mellitus (Revised 2nd ed.). Jaypee Brothers Medical Publishers. 2012. p. 235. ISBN 978-93-5025-489-9. Archived from the original on 14 October 2015.

15. . "The top 10 causes of death Fact sheet  $N^{\circ}310$ ". World Health Organization. October 2013. Archived from the original on 30 May 2017.

16. Rippe RS, Irwin JM, eds. (2010). Manual of intensive care medicine (5th ed.). Wolters Kluwer Health/Lippincott Williams & Wilkins. p. 549. ISBN 978-0-7817-9992-8.

17. Picot J, Jones J, Colquitt JL, Gospodarevskaya E, Loveman E, Baxter L, Clegg AJ (September 2009). "The clinical effectiveness and cost-effectiveness of bariatric (weight loss) surgery for obesity: a systematic review and economic evaluation". Health Technology Assessment. 13 (41): 1–190, 215–357,

iii-iv.doi:10.3310/hta13410.hdl:10536/DRO/DU:30064294.PMID19726018.

18. Cash, Jill (2014). Family PracticeGuidelines (3rd ed.). Springer. p. 396. ISBN 978-0-8261-6875-7. Archived from the original on 31 October 2015.

19. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. (December 2012). "Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010". Lancet. 380 (9859): 2163–96.doi:10.1016/S0140-6736(12)61729-2. PMC6350784. PMID23245607.

20. "What is Diabetes?". Centers for Disease Control and Prevention. 11 March 2020. Retrieved18May2020.

21. "The top 10 causes of death".www.who.int. Retrieved 18 May 2020.

22. American Diabetes Association (2018-03-22). "Economic Costs of Diabetes in the U.S.in2017".DiabetesCare.41(5):917–928.doi:10.2337/dci18-0007.ISSN0149-5992.PMC5911784.PMID29567642.

23. "Deaths and Cost | Data & Statistics | Diabetes | CDC". cdc.gov. 20 February 2019. Retrieved 2 July 2019.

24. Cooke DW, Plotnick L (November 2008)."Type 1 diabetes mellitus in pediatrics". Pediatrics in Review. 29 (11): 374–84, quiz 385. doi:10.1542/pir.29-11-374. PMID18977856. S2CID 20528207.

25. "WHO | Diabetes mellitus". WHO. Retrieved 2019-03-23.

26. Rockefeller, J.D. (2015). Diabetes: Symptoms, Causes, Treatment and Prevention.ISBN978-1-5146-0305-5.

27. Kitabchi AE, Umpierrez GE, Miles JM,Fisher JN (July 2009).
"Hyperglycemic crises in adult patients with diabetes". Diabetes Care. 32 (7):
1335–43.doi:10.2337/dc09-9032. PMC2699725.PMID19564476. Archived from the original on 2016-06-25.

28. Kenny C (April 2014). "When hypoglycemia is not obvious: diagnosing and treating under-recognized and undisclosed hypoglycemia". Primary Care Diabetes. 8 (1): 3–11.doi:10.1016/j.pcd.2013.09.002.PMID24100231.

29. Verrotti A, Scaparrotta A, Olivieri C, Chiarelli F (December 2012). "Seizuresand type 1 diabetes mellitus: current state of knowledge". European Journal of Endocrinology. 167 (6): 749–58.doi:10.1530/EJE-12-0699.

#### PMID22956556.

30. "Symptoms of Low Blood Sugar". WebMD. Archived from the original on 18 June 2016. Retrieved 29 June 2016.

31. "Glucagon–Injection side effects, medical uses, and drug interactions". MedicineNet. Retrieved 2018-02-05.

32. Sarwar N, Gao P, Seshasai SR, Gobin R, Kaptoge S, Di Angelantonio E, Ingelsson E, Lawlor DA, Selvin E, Stampfer M, Stehouwer CD, Lewington S, Pennells L, Thompson A, Sattar N, White IR, Ray KK, Danesh J (June 2010). "Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective

studies".Lancet.375(9733):2215–22.doi:10.1016/S0140-6736(10)60484 9.PMC2904878. PMID20609967.

33. O'Gara PT, Kushner FG, Ascheim DD, Casey DE, Chung MK, de Lemos JA, Ettinger SM, Fang JC, Fesmire FM, Franklin BA, Granger CB, Krumholz HM, Linderbaum JA, Morrow DA, Newby LK, Ornato JP, Ou N, Radford MJ, Tamis- Holland JE, Tommaso CL, Tracy CM, Woo YJ, Zhao DX, Anderson JL, Jacobs AK, Halperin JL, Albert NM, Brindis RG, Creager MA, DeMets D, Guyton RA, Hochman JS, Kovacs RJ, Kushner FG, Ohman EM, Stevenson WG, Yancy CW (January 2013). "2013 ACCF/AHA guidelineforthemanagementofST-

elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines".

Circulation.127(4):e362–425. doi:10.1161/CIR.0b013e3182742cf6.PMID23247304.

34. "Diabetes Programme". World Health Organization. Archived from the original on 26 April 2014. Retrieved 22 April 2014.

35. "Diabetes – eye care: MedlinePlus Medical Encyclopedia". medlineplus.gov. Retrieved 2018-03-27.