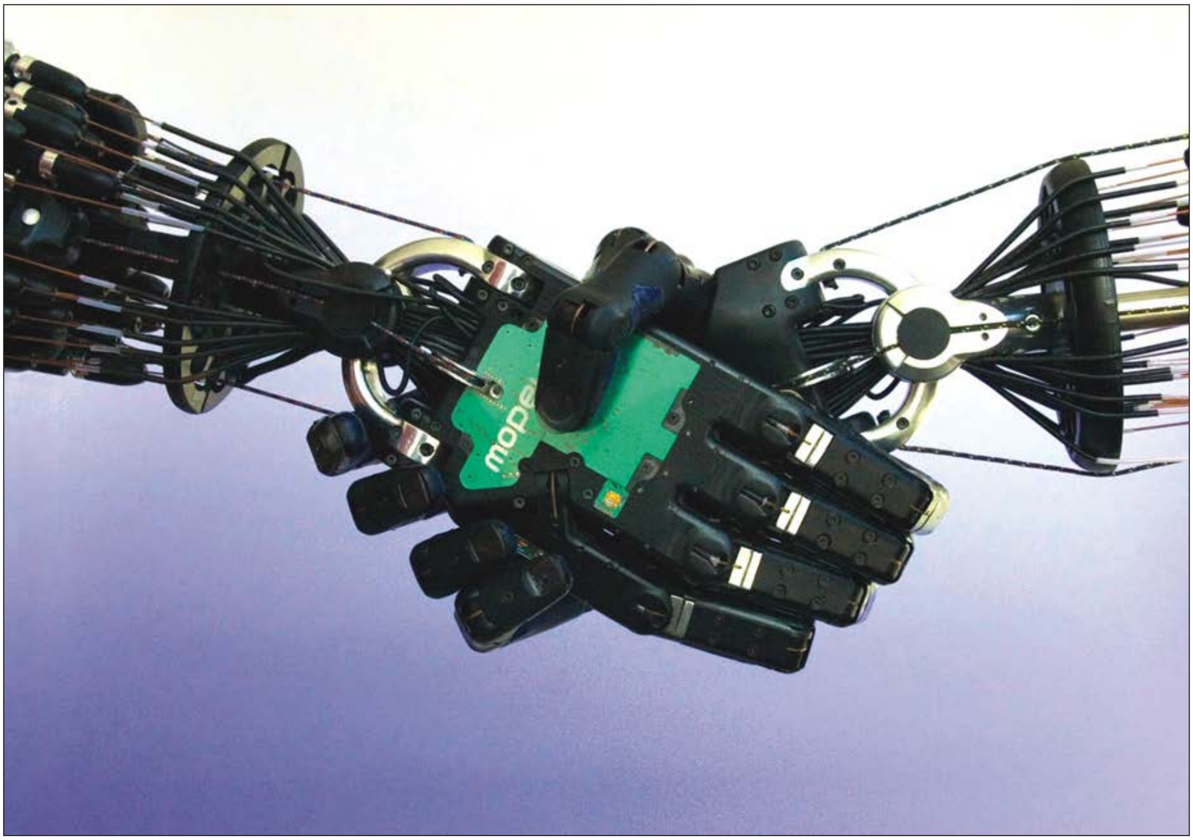

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An Expert System for Endocrine Diagnosis and Treatments using JESS

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Abstract: The aim of the this study was to introduce the design of an expert system which was able to fully diagnoses and treat Pancreas, Thyroid and Parathyroid glands diseases; furthermore, it gave first aids in emergency cases caused by diabetes. Since, diabetes diseases are widely spreads in Gaza, we chose it to be the primary target from the endocrine diseases. Our expert system was not meant to replace the human physician but using such system may be useful in cases like overcoming the problems of the shortage in human physicians and accuracy and speed in processing facts. This system can be used to help the physician in their work. Our expert system was initially evaluated with existing classical test cases. The result of the evaluation was accurate and promising.

Key words: Artificial intelligence, expert systems, JESS, diabetes diseases, endocrine diseases

INTRODUCTION

The endocrine system is classified to be among the most important systems in the human body show the endocrine system (Fig. 1), the glands of the endocrine system and the

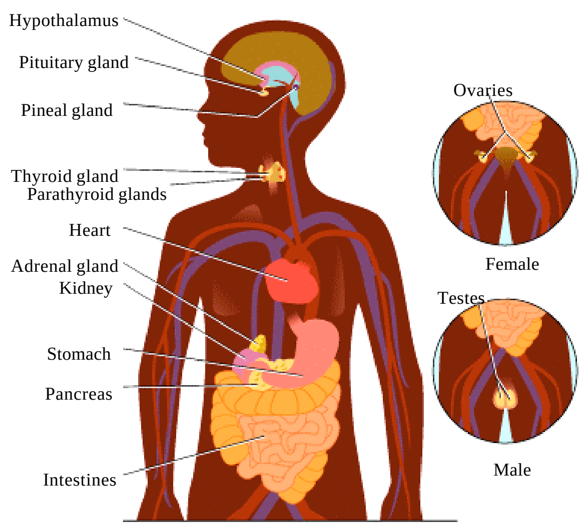

Fig. 1: Endocrine system

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hormones they release not only influence organs in human body but also influence every cell and the overall functions of our bodies. Most diseases nowadays are mainly caused by the inadequate performance of the endocrine system, regulating mood, sexual function, metabolism and growth are all depends on the functionality of the endocrine system.

Generally, the endocrine system is in charge of the body processes that occur slowly, such as cell growth. Faster processes similar to breathing and body movement are managed by the nervous system. But even though the nervous system and endocrine system are distinct systems, they frequently work together to help the body function appropriately (www.kidshealth.org/parent/general/bodybasics/endocrine.html).

Due to the importance of the Endocrine system, we designed and developed an expert system for the followings:

- Diagnosing cases related to Pancreas, Thyroid and Parathyroid glands' diseases and give possible treatments
- Helping newly graduated physician in diagnoses patients' cases and learn from it
- Physicians could use the system to follow up with their patients' treatments or to use for the very urgent cases
- Concession students can use the expert system for training instead of going to the hospitals which are always busy and can't bear a large number of students
- In ambulances the expert system can be used to serve urgent cases of fainting
- In emergency when all physicians are busy with other cases

Artificial Intelligence (AI) is a subfield of computer science concerned with symbolic reasoning and problem solving (Russel and Norvig, 2002; Abu-Naser *et al*., 2008). Expert Systems (ES) which is a branch of AI are computer systems that applies reasoning methodologies to knowledge in a specific domain to render advice or recommendation much like a human expert (Durkin, 1994; Giarratano and Riley, 2004; Jackson, 1999).

In our expert system we use the Java Expert System Shell (JESS) to perform its functions, facts and procedures. It is a rule based engine for the Java language platform which is a superset of CLIPS programming language developed by Ernest Friedman-Hill of Sandia National Lab. (Giarratano, 2002). It was first written in late 1995. It provides rule-based programming suitable for automating an expert system and is often referred to as an expert system shell. In recent years, intelligent agent systems have been developed also, which depend on a similar capability. This system requires having Java version 1.6.0 02 or 1.5.0 running on Windows XP SP2 or Windows Vista Home Premium.

MYCIN

It was the first well known medical expert system developed by Shortliffe at Stanford University (Buchanan and Shortliffe, 1984) to help doctors, not expert in antimicrobial drugs, prescribe such drugs for blood infections. The limitation of MYCIN was: its knowledge base is incomplete since, it does not cover anything like the full spectrum of infectious diseases. Running it would have required more computing power than most hospitals could afford at that time (1976). Doctors do not relish typing at the terminal and require a much better user interface than that provided one.

Easy Diagnosis

It is an expert system software that provides a list and clinical description of the most likely conditions based on an analysis of your particular symptoms (Martin, 2004). Easy diagnosis focuses on the most common medical complaints that account for the majority of physician visits and hospitalizations.

Easy Diagnoses

It is a poorly designed user-interface, the user is required to answer a large number of questions without any notion that gives him the feeling that his data is accepted and will be diagnosed.

PERFEX

It is a medical expert system that support solving problems clinicians currently have in evaluating perfusion studies (Ezquerra *et al*., 1992). The heart of the PERFEX system is the knowledge base, containing over 250 rules. They were formulated using the expertise of clinicians and researchers at Emory University Hospital. PERFEX limitation resides in its output. It is mostly numerical.

INTERNIST-I

It is a rule-based expert system designed at the University of Pittsburgh in 1974 (Kumar *et al*., 2009) for the diagnosis of complex problems in general internal medicine.

ONCOCIN

It is a rule-based medical expert system for oncology protocol management (Wiederhold *et al*., 2001) developed at Stanford University. Oncocin was designed to assist physicians with the treatment of cancer patients receiving chemotherapy.

Dxplain

It is a decision support system which uses a set of clinical findings (signs, symptoms, laboratory data) to produce a ranked list of diagnoses which might explain (or be associated with) the clinical manifestations (Elhanan *et al*., 1996). The DXplain provides justification for why each of these diseases might be considered, suggests what further clinical information would be useful to collect for each disease and lists what clinical manifestations, if any, would be unusual or a typical for each of the specific diseases.

PUFF

It is an expert system for the interpretation of pulmonary function tests for patients with lung disease (Aikins *et al*., 1983). PUFF was probably the first AI system to have been used in clinical practice.

Those Expert Systems suffer from limitation, bad interface or output format.

Our expert system is specialized in the diagnosis of endocrine system diseases with descriptive output and carefully designed interface.

KNOWLEDGE ACQUISITION

Basic information about the endocrine diseases, symptoms and treatment where collected from experts (physicians), books, sites and special prepared notes by clinical physicians. Knowledge elicitation was performed through interviews.

KNOWLEDGE REPRESENTATION

The environment of the system may affect its reliability. The use of some Expert System programming languages make the system limited in specific features.

In our expert system, we used the Java Expert System Shell (JESS) to perform its functions, facts, rules and procedures. JESS is a rule based engine for the Java platform and it is a superset of CLIPS programming language. CLIPS (C Language integrated production System) was developed by Ernest Friedmanhill of Sandia National Labs (Giarratano, 2002). It was originally written in late 1995 and provided rule-based programming suitable for automating an expert system and is often referred to as an expert system shell. The following rule is an example of how knowledge is represented in CLIPS:

- (defrule IDDM
  (Patient (name ?first ?last)(age ?age)) (test (< ?age 30)) (BPressure Hypotension) (Symptoms (ketonuria yes)) (exists (or (Symptoms (coma yes)) (Symptoms(CrackedLips yes)) (Symptoms(Tachycardia yes)) (Symptoms (Confusion yes) (Symptoms (polyuria yes) (polydipsia yes) (polyphygia yes)))))
  =>
  (assert (Type (type IDDM)))
  (printout t ?first" "?last " Has Diabetes type 1" crlf))

Currently, our expert system has more than 60 rules which cover: Pancreas, Thyroid and Parathyroid diseases of the endocrine system. Here, is a brief identification of each of the three diseases that our expert system can help the user with:

Pancreas Diseases

The pancreas is a pinkish-grey organ that lies behind the stomach. The organ is approximately 15 cm in length with a long, slender body connecting the head and tail segments (Kumar *et al*., 2004; Martini, 2001; Moore *et al*., 2009).

The endocrine pancreas is separate from the exocrine pancreas. The endocrine pancreas is made up of small clumps of cells within the pancreas, called pancreatic islets, or the islets of Lange Hans. These account for only 1% of the pancreatic mass. It is composed of three distinct cell types each producing a different hormone. The two important hormones are:

- **Glucagon:** Secretion of glucagon is controlled by the level of blood sugar, being released when levels are too low. This greatly increases the output of sugar from the liver and returns blood sugar levels to normal
- **Insulin:** Insulin is needed to convert sugar (glucose), starches and other food into energy needed for daily life. Insulin is designed to lower blood sugar levels when they become too high and is released in periods when there is a lot of sugar available, like after a meal

Hyperglycaemia

Diabetes Mellitus is a clinical syndrome characterized by hyperglycaemia due to absolute or relative deficiency of insulin. Lack of insulin, whether absolute or relative, affects the metabolism of carbohydrates, protein, fat, water and electrolytes. The Hyperglycaemia is introduced in terms of increasing the glucose in the blood. That means that there is no insulin to reduce the percent of the glucagose to its normal level.

Classification of Diabetes Mellitus

Insulin-Dependent Diabetes Mellitus (IDDM) is called the type one that means it is the first type of diabetes mellitus and this type has characteristics that different from the second one (Bryant *et al*., 2006).

Table 1: Classification of diabetes mellitus

Type	Examples
Primary	
1- Type I (IDDM)	
2- Type II (NIDDM	
Secondary To other pathology	
1- Pancreatic pathology	Pancreatitis
	Haemochromatosis
	Neoplastic disease
	Pancreatectomy
	Cystic fibrosis
2-Excess endogenous production of hormonal antagonists to insulin	Growth hormone (acromegaly)
	Glucocorticoids (Cushing's syndrome)
	Thyroid hormones (hyperthyroidism)
	Catecholamines (phaeochromocytoma)
	Human placental lactogen (pregnancy)
	Glucagon (glucagonoma)
	Counterregulatory hormones (severe burns, trauma)
3- Medication with	Corticosteroids
	Thiazide diuretics
	Phenytoin
4- Liver disease	
Associated with genetic syndromes	DIDMOAD (i.e., diabetes insipidus,diabetes mellitus, optic atrophy, nerve deafness)
	Lipoatrophy
	Muscular dystrophies
	Friedreich's dystrophies
	Down syndrome
	Klinefelter's syndrome
	Turner's syndrome

The patients with IDDM depend on the insulin in their treatments. Death may results from the absolute deficiency of insulin, so the patients must take the insulin to stay alive. Most IDDM's patients are from children and young people.

The second type of primary diabetes mellitus is the Non-Insulin-Dependent Diabetes Mellitus (NIDDM).

The patients under this type have relative deficiency of insulin and they may take drugs or make diets as treatments (Bryant *et al*., 2006). That does not mean that they do not take insulin but the insulin is the last choice that may be needed overtime. Most patients in this type are obese and old (Table 1) under excess endogenous production of hormonal antagonists to insulin topic, the probable actions of hormones countering the effect of insulin in humans.

Diagnostic Criteria for Diabetes Mellitus

Persons presented with clinical manifestations that are normally associated with diabetes (such as polyuria, polydipsia, weight loss and blurred vision) and/or major risk factors for diabetes, should be referred to the laboratory for fasting plasma glucose (Rajala *et al*., 1995; Garancini *et al*., 1995).

Hypoglycaemia

Hypoglycaemia, defined as a blood glucose concentration of less than 2.5 mmol L^{-1}, occurs commonly in diabetic patients treated with insulin and relatively infrequently in those taking a Sulphonylureas drug (Cryer, 2001; Cryer *et al*., 2009). In most instances the patient has no difficulty in recognizing the symptoms of hypoglycaemia and can take appropriate remedial action. However, in certain circumstances (e.g., during sleep) and particularly in certain type of patients (e.g., patients with long duration of IDDM) warning symptoms are not always perceived by the patient even when awake so that appropriate action is not taken and if no assistance is available, unconsciousness is the result. Severe hypoglycaemia, defined as hypoglycaemia requiring the assistance of another person for recovery, can result in serious morbidity and has recognized mortality of 2 to 4% in insulin-treated patients. The unrecognized mortality is probably significantly higher than this. Sudden death in sleep otherwise healthy young patients with IDDM has been described and has been attributed to hypoglycaemia-induced cardiac arrhythmia.

Recurrent severe hypoglycaemia is very disruptive and impinges on many aspects of the patient's life including employment, driving and sport. Risk of hypoglycaemia is the most important single factor limiting attainment of the therapeutic goal, namely normal/near normal glycaemia in patients with IDDM.

Causes of Hypoglycaemia

The main causes of hypoglycaemia in patients taking insulin or a Sulphonylureas drug are as follows (Cryer, 2001; Cryer *et al*., 2009):

- Missed, delayed or inadequate meal
- Unexpected or unusual exercise
- Alcohol
- Poorly designed insulin regime, particularly that predisposing to nocturnal hypoglycaemia
- Defective glucose counter-regulation/unawareness of hypoglycaemia
- Gastroparesis due to autonomic neuropathy
- Other endocrine disorder, e.g., Addison's disease
- Malabsorption
- Factitious hypoglycaemia
- Other causes include the following:
  GI surgery, Idiopathic, Hepatic disease, Islet cell tumor/extrapancreatic tumor, Exercise (in diabetic patients), Pregnancy, Renal Glycosuria, Ketotic hypoglycemia of childhood, Adrenal insufficiency, Hypopituitarism, Enzyme deficiency, Large tumors (e.g., mesenchymal tumors, epithelial tumors, endothelial tumors), Sepsis, Starvation and Artifact

Symptoms of Hypoglycaemia

The symptoms of hypoglycaemia fall into two main groups (Cryer, 2001; Cryer *et al*., 2009) those related to acute activation of the autonomic nervous system and those secondary to glucose deprivation of the brain (neuroglycopenia). They are categorized as follows:

- Autonomic (Sweating, Trembling, Pounding heart, Hunger, Anxiety)
- Neuroglycopenic (Confusion, Drowsiness, Speech, difficulty, Inability to concentrate, Incoordination)
- Non-specific (Nausea, Tiredness, Headache)

Diabetic Ketoacidosis

Prior to the discovery of insulin more than 50% of diabetic patients died in ketoacidosis (Eledrisi *et al*., 2006; Powers, 2005). Today this complication should account for less than 2%

of deaths among diabetics. However, both the incidence and the mortality rate are still unfortunately high. Failure of patient to understand the disease and to appreciate the significance of symptoms of poor control is the most common causes. Its prevention is largely a matter of education of both patients and doctors. A significant number of new patients still present in diabetic ketoacidosis and in established diabetics a common course of events that patients may develop: intercurrent infection, lose of their appetite and either stop or drastically reduce their dose of insulin (on either their own initiative or their doctor's advice) by mistakenly belief that under these circumstances less insulin is required. Any form of stress, particularly which produced by infection, may precipitate severe ketoacidosis in even mildest case of diabetes.

Thyroid Disease

The thyroid is a small gland; shaped likes a butterfly that rests in the middle of the lower neck (Fig. 1). Its primary function is to control the body's metabolism (rate at which cells perform duties essential to living). To control metabolism, the thyroid produces hormones, T4 and T3, which tell the body's cells how much energy to use (Fatourechi, 2009; Villar *et al*., 2007).

A properly functioning thyroid will maintain the right amount of hormones needed to keep the body's metabolism functioning at a satisfactory rate. As the hormones are used, the thyroid creates replacements. The quantity of thyroid hormones in the bloodstream is monitored and controlled by the pituitary gland. When the pituitary gland, which is located in the center of the skull below the brain, senses either a lack of thyroid hormones or a high level of thyroid hormones, it will adjust its own hormone (TSH) and send it to the thyroid to tell it what to do. When the thyroid produces and releases more hormones than ones body needs, it is called Hyperthyroidism.

Parathyroid Disease

Parathyroid glands are small glands of the endocrine system which are located in the neck behind the thyroid (Fig. 1). There are four parathyroid glands which are normally the size and shape of a grain of rice (Eknoyan, 1995). Occasionally, they can be as large as a pea and still be normal. Normal parathyroid glands are the color of spicy yellow mustard. Although, the thyroid and parathyroid are neighbors and both are part of the endocrine system, they are unrelated and do not have the same functions. Hyperparathyroidism is the principle disease of parathyroid glands. It occurs when one of the parathyroids develops a tumor which makes too much parathyroid hormone.

Expert System User Interface

Communication between the user and the expert system is done through the user interface which was implemented in Arabic and English language to be easy for the regular end user (Fig. 2). The user interface does not require much tying.

When the user choose Clinical Examination for example, a new screen is displayed in the format of a dialogue, the expert systems ask a question and the user choose the best answer form the choices provided (Fig. 3).

Finally, the expert system informs the patient/user about the initial results of consultation of the phase one checkup (Fig. 4).

The expert system and the user as a second phase of checkup is started to determine a more accurate percentage that the user is diabetic (Fig. 5).

The final result of consultation of phase2 is displayed to the user (Fig. 6).

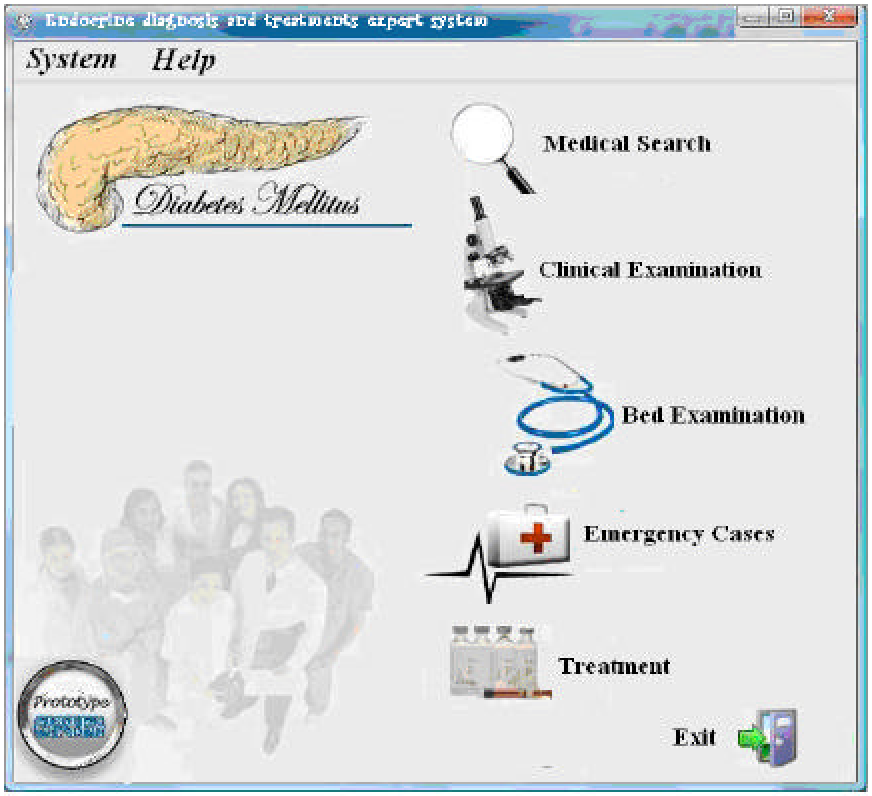

Fig. 2: Expert system user interface

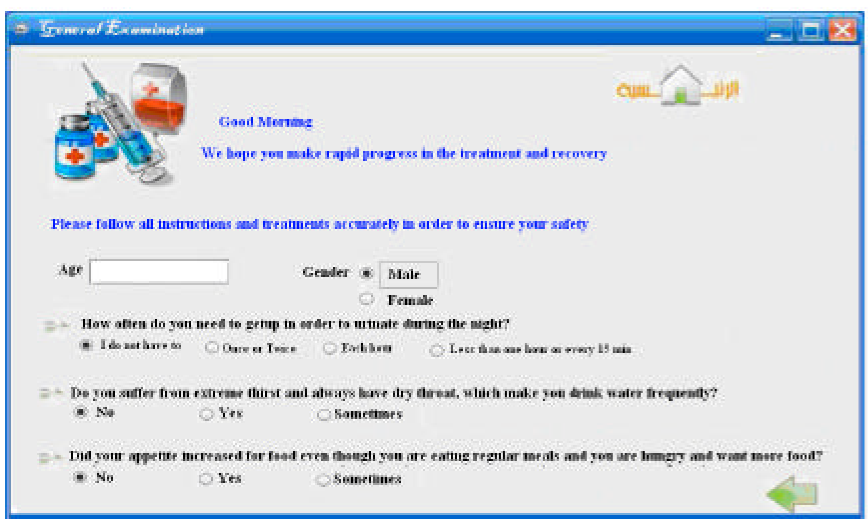

Fig. 3: General examination phase1

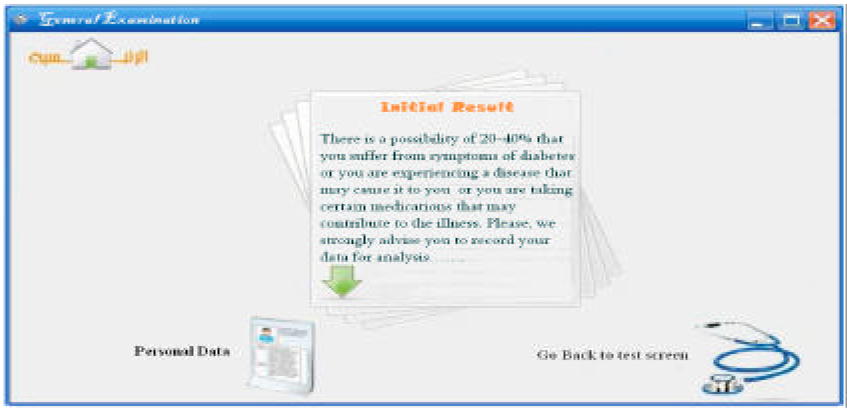

Fig. 4: Initial results of consultation for phase 1

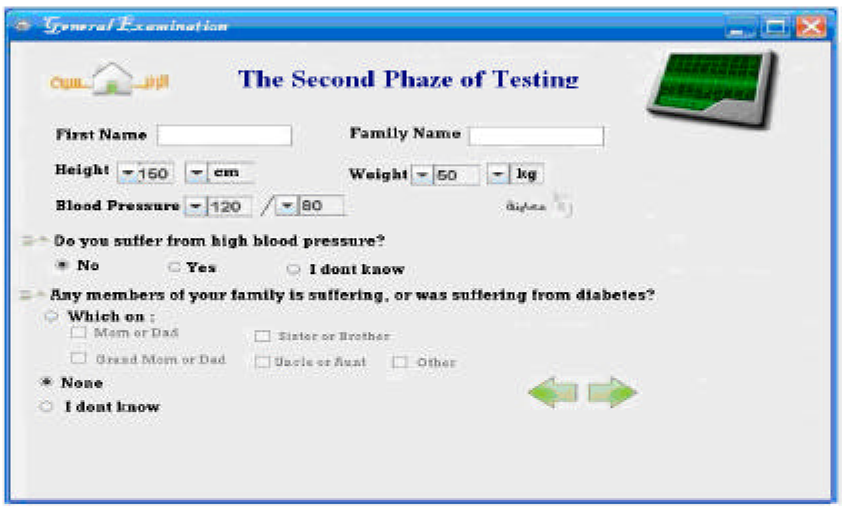

Fig. 5: General examination phase 2

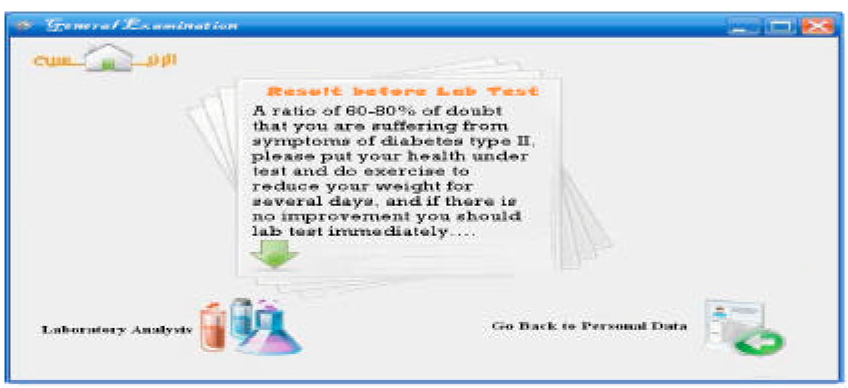

Fig. 6: Results of consultation for phase 2

System Evaluation

In a preliminary evolution of the expert system, a few classical test cases were used to test the expert system and the result of the system was accurate when compared with the result of the Physicians; furthermore, some patients having diabetes diseases tried this expert system, in order to evaluate it and they were surprised by the accuracy of the diagnosis and treatment of the diabetes diseases.

CONCLUSION AND FUTURE WORK

In this study, we have presented a medical expert system for Endocrine Diagnosis and Treatments. Even though, our expert system is similar to some previously implemented experts systems; but we managed to overcome the limitations they had. We have concentrated on three glands: Pancreas with diabetes disease, Thyroid with hyper and hypothyroidism diseases and parathyroid with hyper and hypoparathyroidism diseases. We used Java Expert System Shell (JESS) to perform its functions, facts and procedures. The JESS is a rule based engine for the Java language platform which is a superset of CLIPS programming language. The system can be improved to include more glands and to add more diseases to the system. We have tested the system by using classical diagnosed cases and checked if the system's results in agreement with the physicians diagnoses.

This expert system is considered to be a base of future ones; additional diseases and features like data recording of patients are planned to be added and to make it more accessible to users from anywhere at any time.

EXPERT SYSTEM SOURCE CODE

Part of the facts and rules

```
(deftemplate Patient
(slot age)
(multislot name)
(slot height)
(slot weight)
(multislot bloodPressure)
(slot sex))
(deftemplate Symptoms
(slot retinopathy)
(slot depression)
(slot feetPathy)
(slot nephropathy)
(slot Tendonreflexes)
(slot ketonuria)
(slot familyHistory)
(slot coma)
(slot CrackedLips)
(slot FurredTongue)
(slot Tachycardia)
(slot Confusion))
(deftemplate type
(slot type))
((defrule BMI
```

```
(Patient (name ?first ?last) (weight ?weight) (height ?height))
=>
(assert (bmi (/ ?weight ?height) ?first ?last)))

(defrule underWeight
(bmi ?bmi1 ?first1 ?last1) (test (<= ?bmi1 19.9))
=>
(assert (Obesity underweight)) (printout t ?first1 " " ?last1 " is underWeight with BMI = "
?bmi1 crlf))


(defrule normal
(bmi ?bmi2 ?first2 ?last2) (test (and(>= ?bmi2 20.0) (<= ?bmi2 24.9)))
=>
(assert (Obesity Normal)) (printout t ?first2 " " ?last2 " is Normal with BMI = " ?bmi2 crlf))

(defrule Overweight
(bmi ?bmi3 ?first3 ?last3) (test (and(>= ?bmi3 25.0) (<= ?bmi3 29.9)))
=>
(assert (Obesity Overweight)) (printout t ?first3 " " ?last3 " is Overweight with BMI = " ?bmi3
crlf))

(defrule Obese
(bmi ?bmi5 ?first5 ?last5) (test (and(>= ?bmi5 30.0) (<= ?bmi5 39.9)))
=>
(assert (Obesity Obese)) (printout t ?first5 " " ?last5 " is Obese with BMI = " ?bmi5 crlf))

(defrule GrossObese
(bmi ?bmi6 ?first6 ?last6) (test (>= ?bmi6 40.0))
=>
(assert (Obesity GrossObesity)) (printout t ?first6 " " ?last6 " has GrossObesity BMI = "
?bmi6 crlf))

(defrule Hyper
(Patient (name ?first ?last)(bloodPressure ?up ?down)) (test (and(>= ?up 140.0) (>= ?down
90.0)))
=>
(assert (BPressure Hypertension)) (printout t ?first" Has Hypertension" crlf))

(defrule Hypo
(Patient (name ?first ?last)(bloodPressure ?up ?down)) (test (and(<= ?up 80.0) (<= ?down
50.0)))
=>
(assert (BPressure Hypotension)) (printout t ?first" Has Hypotension" crlf))

(defrule NIDDM
(Patient (name ?first ?last)(age ?age)) (test (> ?age 30)) (Obesity Obese — GrossObesity)
(BPressure Hypertension) (Symptoms (ketonuria yes))
(exists (or (Symptoms (retinopathy yes)) (Symptoms (depression yes)) (Symptoms (feetPathy
yes))
```

```
(Symptoms (nephropathy yes)) (Symptoms (Tendonreflexes no)) (Symptoms (familyHistory
yes))))
=>
(assert (Type (type NIDDM))) (printout t ?first” ”?last ” Has Diabetes type 2” crlf))

(defrule IDDM
(Patient (name ?first ?last)(age ?age)) (test (< ?age 30)) (BPressure Hypotension) (Symptoms
(ketonuria yes))
(exists (or (Symptoms (coma yes)) (Symptoms(CrackedLips yes)) (Symptoms(Tachycardia
yes))
(Symptoms (Confusion yes))))
=>
(assert (Type (type IDDM))) (printout t ?first” ”?last ” Has Diabetes type 1” crlf))

(deffacts Cases (Patient (name Rami Abd)(age 40)(weight 60)(height 2)(bloodPressure 140
95))
(Patient (name Ali Ahmed)(age 20)(weight 30) (height 2) (bloodPressure 80 50))
(Patient (name Sami Deib)(age 10)(weight 40) (height 2) (bloodPressure 90 70))
(Symptoms (coma yes) (CrackedLips yes) (Tachycardia yes) (Confusion yes) (ketonuria yes))
(Symptoms (retinopathy yes) (depression yes) (feetPathy yes) (nephropathy yes)
(Tendonreflexes no) (ketonuria no) (familyHistory yes)))
```

REFERENCES

Abu-Naser, S.S., K.A. Kashkash and M. Fayyad, 2008. Developing an expert system for plant disease diagnosis. J. Artif. Intell., 1: 78-85.

Aikins, J.S., J.C. Kunz, E.H. Shortliffe and R.J. Fallat, 1983. PUFF: an expert system for interpretation of pulmonary function data. Comput. Biomed. Res., 16: 199-208.

Bryant, W., J. Greenfield, D. Chisholm and L. Campbell, 2006. Diabetes guidelines: easier to preach than to practise? A retrospective audit of outpatient management of type 1 and type 2 diabetes mellitus MJA, 185: 305-309.

Buchanan, B.G. and E.H. Shortliffe, 1984. Rule-Based Expert Systems: The MYCIN Experiments of the Stanford Heuristic Programming Project. Addison-Wesley, New York, ISBN-10: 0201101726. pp: 769.

Cryer, P., 2001. Hypoglycemia. In: Handbook of Physiology; Section 7, The Endocrine System. II. The Endocrine Pancreas and Regulation of Metabolism, Jefferson, L., A. Cherrington and H. Goodman (Eds.). American Physiological Society, Oxford University Press, New York, pp: 1057-1092.

Cryer, P.E., L. Axelrod, A.B. Grossman, S.R. Heller, V.M. Montori, E.R. Seaquist and F.J. Service, 2009. Evaluation and management of adult hypoglycemic disorders: an Endocrine Society Clinical Practice Guideline. J. Clin. Endocrinol. Metab., 94: 709-728.

Durkin, J., 1994. Expert Systems: Design and Development. 1st edn., Prentice Hall, Englewood Cliffs, NJ., ISBN 0-02-330970-9.

Eknoyan, G., 1995. A history of the parathyroid glands. Am. J. Kidney Dis., 26: 801-807.

Eledrisi, M.S., M.S. Alshanti, M.F. Shah, B. Brolosy and N. Jaha, 2006. Overview of the diagnosis and management of diabetic ketoacidosis. Am. J. Med. Sci., 331: 243-251.

Elhanan, G., S.A. Socratous and J.J. Cimino, 1996. Integrating DXplain into a clinical information system using the World Wide Web. Proc. AMIA Annual Fall Symp., 96: 348-352.

Ezquerra, N., R. Mullick, E. Garcia, C. Cooke and E. Kachouska, 1992. PERFEX: An Expert System for Interpreting 3D Myocardial Perfusion, Expert Systems with Applications. Pergamon Press, New York.

Fatourechi, V., 2009. Subclinical hypothyroidism: an update for primary care physicians. Mayo Clin. Proc., 84: 65-71.

Garancini, M.P., G. Calori, G. Ruotolo, E. Manara and A. Izzo *et al*., 1995. Prevalence of NIDDM and impaired glucose tolerance in Italy: an OGTT-based population study. Diabetologia, 38: 306-313.

Giarratano, J.C., 2002. CLIPS User's Guide, Software Technology Branch. Version 6.20, NASA Lyndon B. Johnson Space Center, Houston, TX.

Giarratano, J. and G. Riley, 2004. Expert Systems: Principles and Programming. 4th Edn., Thomson/PWS Publishing Co., Boston, MA., ISBN: 0534937446.

Jackson, P., 1999. Introduction to Expert Systems. 3rd Edn., Addison Wesley Longman, Harlow, England, ISBN-10: 0201876868.

Kumar, V., M. Fausto and A. Abbas, 2004. Robbins and Cotran Pathologic Basis of Disease. 7th Edn., WB Saunders Co., New York, ISBN-10: 0721601871. pp: 1552.

Kumar, A.K., Y. Singh and S. Sanyal, 2009. Hybrid approach using case-based reasoning and rule-based reasoning for domain independent clinical decision support in ICU. Expert Syst. Appl. Int. J., 36: 65-71.

Martin, F., 2004. Medical Diagnosis: Test First, Talk Later?. Mathemedics, Inc., USA.

Martini, F.H., 2001. Fundamentals of Anatomy and Physiology. 5th Edn., Upper Saddle River, Prantice Hall, ISBN: 9780130901378.

Moore K., A. Dalley and A. Agur, 2009. Clinically Oriented Anatomy. 6th Edn., Lippencott Williams and Wilkins, UK.

Powers, A., 2005. Diabetes Mellitus. In: Kasper, D.L., E. Braunwald and A.S. Fauci *et al*. (Eds.). Harrison's Principles of Internal Medicine, McGraw-Hill, New York, pp: 2152-2180.

Rajala, U., S. Kiukaanniemi, A. Uusimaki and S. Kivela, 1995. Prevalence of diabetes mellitus and impaired glucose tolerance in a middle-aged Finnish population. Scand. J. Prim. Health Care, 13: 222-228.

Russel, S.J. and P. Norvig, 2002. Artificial Intelligence: A Modern Approach. 2nd Edn., Prentice Hall Pub., ISBN: 0137903952.

Villar, H.C., H. Saconato, O. Valente and A.N. Atallah, 2007. Thyroid hormone replacement for subclinical hypothyroidism. Cochrane Database Syst. Rev., 18: 3419-3419.

Wiederhold, G., E. Shortliffe, L. Fagan and L. Perreault, 2001. Medical Informatics: Computer Applications in Health Care and Biomedicine. 2nd Edn., Springer, New York, ISBN-10: 0387984720. pp: 854.