1.1 Artificial intelligence

Artificial intelligence is a subpart of computer science, concerned with, how to give computers the sophistication to act intelligently, and to do so in increasingly wider realms. It is the name of the academic field of study which studies how to create computers and computer software that are capable of exhibiting intelligent behaviour. It is usually defined as "the study and design of intelligent agents", in which an intelligent agent is a system that perceives its environment and takes actions that maximize its chances of success (Calis et al., 2015). Artificial Intelligence deals with developing algorithms and techniques that can solve the problems in a more human like fashion. The term “Artificial Intelligence” was coined by John McCarthy in 1955, who defined it as the “Science and Engineering of making Intelligent Machines, especially intelligent computer programs” (Serenko et al., 2011). The field was established on the claim that the main property of humans, Intelligence—can be mimicked by a machine. Artificial Intelligence is sometimes also referred to as “Synthetic Intelligence” and is concerned with the computational understanding of what is commonly called - intelligent behaviour and with the creation of artifacts that exhibit such behaviour (Lindley CA, 2012). Programs which enable computers to function in the ways that make people seem intelligent are called artificial intelligent systems.

The field of Artificial Intelligence research was founded at a conference on the campus of Dartmouth College in 1956 (McCorduck et al., 2004). The attendees, including John McCarthy, Marvin Minsky, Allen Newell, Arthur Samuel, and Herbert Simon, became the leaders of AI research for many decades (Russell et. al., 2003). They and their understudies composed projects that were astonishing to the vast majority of people: computers programs were winning at games, taking care of polynomial math problems, forming meaningful hypotheses and communicating in English.

Since, long time, even before the advent of digital computers, many scientists were convinced that machines could be made to exhibit intelligent behaviour. It is natural that as soon as computers appeared, researchers began to program them to do things, which were thought to be possible for human mind only such as: solving numerical problems, understanding text English and playing games. Today computers are used for
forecasting weather conditions and simulate extraordinary galactic events like birth of a star etc. Solving these complex problems involve volumes of computational work. Scientists realized that a human mind cannot be pushed beyond a certain limit and thus began working on development of systems, which possess certain level of intelligence, similar to that of human brain. This led to the evolution of the concept of Artificial Intelligence which deals with the basic understanding of Intelligence and some of its most important aspects, such as vision, speech recognition, learning, thinking, decision making etc. Although artificial intelligence is generally associated with Computer Science, but it has many important links with other fields such as Maths, Psychology, Cognition, Biology and Philosophy, among many others (Lamba, 2008).

Artificial intelligence has now days turned into an integral part of the industry, providing most effective solutions for many of the most difficult problems from all walks of daily life.

1.1.1 Definitions of Artificial Intelligence

Some of the formal definitions are as under:

- *The study of how to make computers to do things at which, at the moment people are better.*  
  
  (Rich and Knight, 1991)

- *The art of creating machines that perform functions that require intelligence when performed by people.*  
  
  (Kurzweil, 1990)

- *The branch of computer science that is concerned with the automation of intelligent behaviour.*  
  
  (Luger, 2002)

- *Artificial Intelligence is the study of mental faculties through the use of computational models.*  
  
  (Charniak and McDermott, 1985)

- *Artificial Intelligence is the study of the computations that make it possible to perceive, reason, and act.*  
  
  (Winston, 1992)
The exciting new effort to make computers think ... machines with minds, in the full and literal sense. (Haugeland, 1985)

The automation of activities that we associate with human thinking, activities such as decision-making, problem solving, learning. (Bellman, 1978)

A field of study that seeks to explain and emulate intelligent behavior in terms of computational processes. (Schalkoff, 1990)

The branch of computer science that is concerned with the automation of intelligent behavior. (Luger and Stubblefield, 1993)

1.2 Brief history of Artificial Intelligence

“Thinking machines and artificial beings” (Butler et al., 1863) appear in Greek myths, such as Talos of Crete, the bronze robot of Hephaestus, and Pygmalion's Galatean (McCorduck et al., 2004). It was also widely believed that artificial beings had been created by Jābir ibn Hayyân, Judah Loew and Paracelsus (Buchanan et al., 2005). By the 19th and 20th centuries, artificial beings had become a common feature in fiction. Mechanical or "formal" reasoning has been developed by philosophers and mathematicians since antiquity. The investigation of rationale led directly to the creation of the programmable computerized electronic computer, based on the work of mathematician Alan Turing and others.

Turing's theory of computation suggested that a machine, by shuffling symbols as simple as "0" and "1", could simulate any conceivable act of mathematical deduction (Copeland et al., 2012). The origin of artificial intelligence lies in the earliest days of machine computations. During 1940’s and 1950’s, Artificial Intelligence began to grow with the emergence of the modern computer. In the early 1950’s much work was done on machine-to-machine translation. The seed of natural language understanding were sown then and it is from then, the knowledge representation has eventually developed. The ability of these new electronic machines to store large amounts of information and process at high speeds opened the eyes of the researchers to build systems that could
exhibit human-like abilities. Artificial Intelligence has been studied for decades and is still one of the most elusive subjects in Computer Science. This partly due to how large and nebulous the subject is. Artificial Intelligence ranges from machines really capable of "thinking" to building intelligent algorithms used to play games. It has applications in almost every way we utilize computers in the day to day life. Among the first researchers to attempt to build intelligent programs were Allen Newell, Herbert, A. Simon and Cliff Shaw. Their first well-known program, “Logic Theorist” which they wrote in 1956, was a program that proved statements using the accepted rules of logic and a problem solving program of their own design (Simon et al., 1971). It was the first program deliberately engineered to mimic the problem solving skills of a human being and is called "the first artificial intelligence program". It would eventually prove 38 of the first 52 theorems in Whitehead and Russell's book “Principia Mathematica”, and find new and more elegant proofs for some. This, along with concurrent discoveries in neurology, information theory and cybernetics, inspired a small group of researchers to begin to seriously consider the possibility of building an electronic brain. By the mid of the 1960s, Artificial Intelligence research in the U.S. was vigorously financed by the Department of Defence and research centres had been built up the world over. AI's founders were profoundly optimistic about the future of the new field: Herbert Simon predicted that "machines will be capable, within twenty years, of doing any work a man can do" and Marvin Minsky agreed, writing that "within a generation ... the problem of creating 'artificial intelligence' will substantially be solved" (Herrmann et al., 2009). In the early 1980s, Artificial Intelligence research was revived by the commercial success of Expert Systems, a form of Artificial Intelligence program that simulated the knowledge and analytical skills of one or more human experts. During the last 50 years, science has experienced the realization of many of the visions of the early researchers.

1.3 Intelligence

Intelligence is defined as the ability to acquire, retrieve, and use knowledge in a meaningful way, including both, raw and refined knowledge. It also includes the ability to memorize information, recall facts, and express emotions. The important aspects of human intelligence are:-
• Commonsense,
• Judgement and decision making,
• Problem solving using creativity,
• Use of intuition to make choice of action about the forthcoming events,
• Goal directedness and planning,
• Plausible reasoning,
• Knowledge by experience and set of beliefs.

Even though the human intelligence is powerful, it has some limitations. Humans are intellectually fallible; they have limited knowledge bases, and information processing of a serial nature which proceeds very slowly in brain as compared to that of computers. Therefore, the meaning of intelligence is not human brain’s information processing ability but the ability of humans to demonstrate their intelligence by communicating effectively, and by learning. Humans can acquire knowledge by experience and then demonstrate, by communicating the knowledge that they have acquired. Main stream thinking in psychology considers human intelligence as an ability in-cognitive process. The present research in Artificial Intelligence is focused on the following components of intelligence:- Learning, Reasoning, Understanding, Creativity and Intuition. Researches around the world are aiming to develop computer systems exhibiting the above features and have been successful to certain extent too.

1.4 Learning

The modification of behaviour through practice, training or experiences is called learning which involves detection and correction of errors. An error is the mismatch between our intentions and what actually happens. It refers to the changes in the behaviour of system which are the result of regularities in the environment of that organism. Learning process is the basis of knowledge acquisition process. Knowledge acquisition is the expanding the capabilities of a system or improving its performance at some specified task. So we can say knowledge acquisition is the goal oriented creation
and refinement of knowledge. The acquired knowledge may consist of various facts, rules, concepts, procedures, heuristics, formulas, relationships or any other useful information. Knowledge can be acquired from various sources like, domain of interests, text books, technical papers, databases, reports etc. Learning involves to develop generalization after acquiring experience. A computer system is said to have done learning, if it is able not only do the “repetition of same task” more effectively or at level of efficiency at par with humans, but also the similar tasks in the related domain. Learning occurs due to some refinement of skills by acquisition of knowledge. Refinement of skills refers to the situation of improving the skill by performing the same task again and again.

1.4.1 Supervised learning

Supervised learning algorithms are a class of machine learning algorithms that infer a function from a labelled set of training data which consist of a set of training examples pairs comprising of an input vector and corresponding output vector. These algorithms examine the samples in training set and construct a function that is further used in mapping of new unseen examples. The performance of these algorithm depends on the quality ad quantity of training data, usually in an optimal scenario once these algorithms are trained with enough training samples they are able to correctly determine the class labels for unseen instances.

1.4.2 Unsupervised learning

Unsupervised learning algorithms are a class of machine learning algorithms that infer a function from an unlabelled set of training data by finding the hidden relationships in the structure of data. As the training samples are unlabelled these algorithms doesn’t use a reward or punish signal to evaluate solution as is used in reinforcement learning or supervised learning. These algorithms are closely related to clustering algorithms and density estimation techniques of statistics. In addition to this unsupervised algorithms also include many other procedures that tend to summarize and explain key features of the data.
1.5 Machine Learning

Machine learning is the branch of artificial intelligence which aims at providing computational methods for accumulating, changing and updating knowledge in the intelligent systems. Machine learning techniques are useful in situations where the conventional algorithmic solutions are not successful and there is a lack of formal knowledge about the application domain. Machine learning techniques were from the initial stage so developed as to make them robust for analysis of not only large datasets but also for datasets from a variety of domains. The main focus of machine learning techniques is the design of algorithms that find out complex relationships hidden in the data and make decisions based on them. Many machine learning systems aim at eliminating the need of human intuition in the analysis of data, while as others adopt a collaborative approach between machines and humans. However human intuition cannot be eliminated entirely because the system’s designers need to specify how the data is to be represented and what mechanisms will be used to search the hidden patterns in the data. Machine learning can be seen as located at the intersection between computer science, applied mathematics and statistics sharing concepts with artificial intelligence and information theory. The field has evolved from the study of pattern recognition and computational learning theory in artificial intelligence. Machine learning as a field of study that gives computers the ability to learn without being explicitly programmed. This branch of computer science works for construction of algorithms that can learn to make predictions for new and unseen data by learning on training data. These algorithms work by building a regression model using the training data and fit the test data into that model rather than following strictly conventional static programming.

Algorithms in machine learning involve adaptive mechanisms that facilitate a machine to learn by example, experience and by analogy. Learning capabilities can improve the performance of an intelligent system over time. In machine learning, data
plays an indispensable role, and the learning algorithm is used to discover and learn knowledge or properties from the data. Quality of data plays an important role in the performance of algorithms. Quality of data is measured in terms of precision in obtaining the data and also in terms of relevance to the area of study. Quantity of data also plays an important role in deciding the performance. More diverse a dataset is; such that it covers all of the possible variations in the domain of analysis; more performance the system is expected to deliver. There are two general dataset types. One is labelled and the other one is unlabeled:

- **Labeled dataset** $\mathcal{D}: X = \{x^{(n)} \in R^d\}_{n=1}^N, \quad Y = \{y^{(n)} \in R\}_{n=1}^N$

- **Unlabeled dataset** $\mathcal{D}: X = \{x^{(n)} \in R^d\}_{n=1}^N$

where X denotes the *feature set* containing N samples. Each sample is a d-dimensional vector and called a feature vector or feature sample, while each dimension of a vector is called an attribute, feature, variable, or element. Y stands for the *label set*, recording what label a feature vector corresponds to. In some applications, the label set is unobserved or ignored. In order to examine the performance of learning, another dataset may be reserved for testing, called the *test set* or *test data*. For example, during the classroom sessions or during teaching, the teacher may train students using several problems for learning and practice (training set), and the during exams a teacher may examine the learning of students on the basis of another set of similar but unseen problems (test set).

### 1.6 Expert Systems

An expert system is a computer system that emulates the decision-making ability of a human expert (Jackson et al., 1998). An expert system is a set programs that manipulate encoded knowledge to solve problems in a specified domain that normally require human expertise. Expert systems are designed to solve complex problems by reasoning about knowledge, represented primarily as if–then rules rather than through conventional procedural code. An expert system’s knowledge is obtained from some
expert sources and coded in a form suitable for the system to use in its inference or reasoning processes. The expert knowledge must be obtained from specialists who have gained knowledge and experience for a vast duration of time or other sources of expertise, such as texts, journals, articles and journals. Once the sufficient body of knowledge has been acquired, it must be encoded in some form, loaded into a knowledge base, then tested and refined throughout the life of the system. Expert systems have been built for a variety of purposes including medical diagnosis, electronic fault finding, mineral prospecting and computer system configuration. The inference engine of an expert system works on the knowledgebase to produce inferences. Knowledge acquisition is used to obtain knowledge specific the domain of interest. The general characteristics of an expert system are as given below:

**High performance:** The system should exhibit considerably high level of performance and the quality of advice presented by the system should be of at a level of competency equal to or better than human expert of the domain.

**Expertise:** the expert system should be robust in applying the knowledge and expertise to produce the solutions which are both efficient and effective to solve the problems at hand. In addition it should eliminate the wasteful and unnecessary calculations.

**Adequate response time:** The system should be designed in such a way that it should be able to reach a solution in a reasonable amount of time comparable to or better than the time taken by the human experts.

**Good Reliability:** The expert systems should be reliable as human experts.

**Explanation facility Self-knowledge:** The explanation facility is the knowledge that explains how a system has arrived at the answer presented. The ability to examine the reasoning process and explain the operation is the most important qualities of the expert systems. Explanation facility is important because it tend to build more faith and confidence in the solution presented by the system. This also allows the users to ask the expert system to justify the solution or advice provided.
Flexibility: Although the expert system has a large amount of knowledge, the knowledge is an entity that is ever explaining; as such it is important to have an efficient mechanism to have a mechanism for adding, changing and deleting.

Understandable: The system should be understandable, i.e., be able to explain the steps of reasoning while executing. The system should have an explanation capability similar to that of human experts.

The first expert systems were created in the 1970s and then proliferated in the 1980s (Leondes et al., 2002). Expert systems were among the first truly successful forms of Artificial Intelligence software (Russell et al., 1995)

1.7 Artificial Neural Networks

Artificial neural network (ANN) is a machine learning method inspired and evolved from the structure, function and working of human brain. ANN are data processing systems that are composed of large number of simple, processing elements called neurons, which are highly interconnected (Saxena et al., 2007). These neurons work together and are organised in a sequence of layers in a parallel architecture inspired by the working of cerebral cortex of brain. Well designed neural networks are self-adaptive trainable systems that can often “learn” to solve complex problems from a set of examples and generalize the learning gained and apply the same solve unseen problems of similar nature. Each neural network has three critical components; nodal character, network topology and learning rules. Nodal character determines how signals are processed by the node, such as the number of inputs and outputs associated with the node, weights associated with each input and output and the activation function. Network topology determines the fashion in which the nodes are connected. Learning rules determine how the weights are initialized and adjusted. The input layer is not the neural computing layer because the node doesn’t have the input weights and also they don’t have any activation function. The top layer is the output layer that presents the response for the input fed to the network. The other layers are called the hidden or intermediate layers as they don’t have any connection with the outside world.
Mathematically let $I=(I_1, I_2, \ldots, I_n)$ represent the set of inputs presented to the unit $U$. Each input has an associated weight that represents the strength of that particular connection. Let $W=(W_1, W_2, \ldots, W_n)$ represent the weight vector corresponding to the input vector $X$. By applying to $V$, these weighted inputs produce a net sum at $U$ given by $S = \text{SUM}(W_i \cdot I_n)$. The weights of the connections between the layers of neurons are updated from time to time which depends on the learning function used. A neural network is composed of such units and weighted unidirectional connections between them. In some neural nets, the number of units may be in the thousands. The output of one unit typically becomes an input for another. There may also be units with external inputs and/or outputs.

1.8 **Use of Artificial intelligence in medical diagnosis**

The use of artificial intelligence in medical diagnosis is becoming increasingly popular and has been widely used in the diagnosis of tumours, cancers, hepatitis, lung diseases, etc. The primary concern of machine learning in medicine is construction of artificial intelligent systems that can assert a medical doctor in performing expert diagnosis. These programs by making use of various computational techniques find out the hidden patterns from the training data and using these patterns they classify the test data into one the possible categories. The backbones of these systems are the various data sets prepared from various clinical cases which act as practical examples in training the system. As the domain of medicine is ever expanding it is very difficult for a physician to always stay abreast of medical knowledge outside a narrow field. Consultation with a expert specialist is a solution when the clinical problem lies beyond the physician's competency, but expert opinion is most of the time either not available or available but not in timely fashion for regular follow-ups. Many attempts have been made in past in order to develop computer expert programs that can work as consultants. Mostly these programs have been built using rule-based systems whose knowledge base is recorded in the form of "if – then " rules which are used in series of deduction to arrive at a conclusion (Chaturvedi Anil et al., 2010). In many domains which are quit narrow in domain these rule-based programs have shown a skilled behaviour as good as human expert. Although this is true for some of the constricted domains of medical diagnosis
also, but most of the medical diagnostic problems are so complex and having overlapping
indications that simple rule-based systems fail to perform well and encounter major
difficulties. The main reason of failure of these systems arises primarily from the fact
that these rule-based systems fail to represent clinical reasoning process of humans and as
such are not able to make up a model of disease. In such a situation adding up of new
rules lead to creation of unanticipated and impractical deductions which result in
degradation of performance of programs. Keeping in view the problems encountered with
simple rule-based systems, most recent developments of application of artificial
intelligence in medicine diagnosis have primarily focused on building programs to
develop models of disease. Efforts in the direction of building such programs have led to
considerable advancement in our understanding of expertise decision making of medical
experts, in transforming of such knowledge into cognitive models, and in the translation
of various models into intelligent expert systems. In recent past machine learning has
presented numerous essential tools used for intelligent data analysis. These days the
advanced health care systems are equipped with digital data collection and online
monitoring of patients. This data is collected and shared with other peer information
systems for analysis of this data to find out the hidden trends in the data. Machine
learning technology is best suited for analyzing these large volumes of medical data. The
valuable medical knowledge is often available in the form of past patient medical records
medical health care institutes. All that is needed is to gather and consolidate this
knowledge about correct clinical diagnosis. This consolidated information is further to be
used for training intelligent learning algorithm in order to construct a specialist program.
Although this is an over-simplification of the problem, but in principle, the medical
diagnostic knowledge can be automatically derived from the account of cases solved in
the past. The intelligent program developed using the knowledge base so gained, can
thereafter be used either to assist the medical doctor for diagnosing new cases so as to
achieve better and timely diagnosis, with increased accuracy and reliability. The same
can also be used to train students or medical technicians to screen or diagnose patients in
special diagnostic problems.

1.9 Cancer
“Cancer”\(^1\) is an umbrella term that covers a large family of diseases which primarily involve abnormal and uncontrolled growth of cells which have potential to spread to other parts of body also. These cells which have undergone unregulated growth form a lump of mass called tumour or neoplasm. All tumour cells demonstrate six signs of cancer. These are the basic features that the cancer cells need to show so as to produce a malignancy. These include:- Cell division and growth without any signal to do so, continued growth of cells and cell multiplications even when there are signals to stop further growth/multiplication. Avoidance of programmed cell death, Continuous and unbounded cell divisions, Promoting blood vessel construction, Invasion of other tissue and formation of metastases. The process of gradual conversion of normal healthy cells into cells that can cancerous cells involves several steps known as malignant progression. In the initial stage of cancer usually no symptoms are realised. Signs and symptoms only begin to appear when the undesired mass begins to grow in size and these indications are dependent on the type of cancer and the organ which is affected. A small number of symptoms are specific, and most of them are overlapping with many other frequently occurring diseases. For this reason Cancer is said to be a “great imitator”. This is not uncommon for people diagnosed with cancer to have been treated for other diseases, which were assumed to be causing the observable symptoms. Initial growth of mass if usually painless but in advanced stages localised pain may occur. Sometimes local symptoms occur due to the growth of the mass of tumour or due to its ulceration. For instance due to the growth of the mass of the tumour of lung cancer may cause blockage of the bronchus which may result in cough or pneumonia; cancer in the oesophageal region can cause narrowing of the passage of oesophagus which may make it difficult or pain in swallowing and colorectal cancer may cause narrowing or even blockages in the bowel, which may result in result in changes in bowel habits. Ulceration can result in bleeding, and if it occurs in lungs will lead to coughing up of blood, if ulceration occurs in bowels may cause rectal bleeding or anaemia, in the bladder may lead to blood in the urine, and in the uterus to vaginal bleeding. In addition to these, some general symptoms occur due to remote effects of cancer which are not related to metastatic or direct effects of cancer. These symptoms include: changes to the skin, weight loss, fever and being

1.9.1 Metastasis

The spread of a cancer or other disease from one organ to another organ or one part of the organ to another, not directly connected to it is known as Metastasis. Cancer can spread from its original site by local spread, lymphatic spread to regional lymph nodes or by blood (haematogenous spread) to distant sites, known as metastasis. When cancer spreads by a haematogenous route (i.e through blood), it usually spreads all over the body. However, cancer 'seeds' grow in certain selected site only as hypothesized in the “soil and seed hypothesis” of cancer metastasis (Fidler et al., 2003). The symptoms of metastatic cancers depend on the location of the tumor, and can include enlarged lymph nodes, enlarged liver or enlarged spleen, which can be felt in the abdomen, pain or fracture of affected bones, and neurological symptoms.

1.9.2 Causes of Cancer

The vast majority of cancers, almost 90 to 95% of cases are attributed to environmental factors and the remaining 5 to 10% of cases are attributed to inherited genetics (Anand P et al., 2008). Environmental factors are sum-total of all the factors that are not inherited genetically which usually include lifestyle, behavioural and economic factors. The common environmental factors that add to cancer mortality are obesity (30 to 35%), use of tobacco (20 to 30%), eating habits, ionising and non-ionising radiations (up-to 10%), lack of physical activity and environmental pollutants (Anand P et al., 2008). Usually most of the cancers have multiple causes; as such it is nearly impossible to precisely prove what caused a cancer to occur. For instance; if a person who uses tobacco is diagnosed with lung cancer, then although it is most probable that the cancer was caused because of the use of tobacco, but as a result of air pollution everyone has a little chance of developing lung cancer, so there is a small chance that the cancer might have caused because of air pollution.
1.9.3 Cervical cancer

Cervical cancer is malignant tumour that occurs when the cervix tissue cells begin to grow and replicate abnormally without controlled cell division and cell death. In such a state, the body is unable to use and manage such cells for carrying out usual function as a result of which these cells transform into a tumour. If the tumour is malignant, its cell flow through the blood stream and spread to other parts of body, as a result those parts also get infected. Usually the cervical cancer takes number of years to develop. These infected cells are then distinguished as cervical intra-epithelial neoplasia (CIN) or cervical dysplasia. The cells over the surface of cervix that show unusual changes & potentially precancerous developments are called CIN. In most of the cases, CIN do not cause symptoms or disease and are resolved spontaneously by host’s immune system response. However, some CIN may lead to precancerous lesions and if untreated, these lesions may progress to cervical cancer, but this progression usually takes many years. Timely and precise diagnosis of cervical cancer is an important real-world medical problem. Cervical cancer has turn into one of the main causes of mortality among women around the globe and it has become a major concern among the scientific community to investigate into it, leading to early diagnosis and mitigated mortality rate. Cervical cancer is the fourth most common cancer in women, and the seventh overall in the world. As reported by WHO the toll of cervical cancer in 2012 was 528000 with the number of deaths equal to 2660002. A large majority of these cases (around 84%) are reported from the developing and under-developed countries as compared to the developed countries, which is attributed to comparatively poor access to screening and treatment services (Kent A, 2010). The cervical cancer etiology is still not clear and medical experts have not come up with a single dominant cause. Prevention is not so unproblematic and early detection is the only means to help the patients to survive. If the cancerous cells are detected before spreading to other organs, the survival rate for patients is more than 97%. Studies have found that CIN usually results from a virus called human papillomavirus (HPV) which is generally sexually transmitted. There are more than 120 types of HPV known (Chaturvedi Anil et al., 2010) out of which only 15 are classified as high-risk types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82), 3 as probable-high-

2 http://globocan.iarc.fr/old/FactSheets/cancers/cervix-new.asp; retrieved on 10-10-2016
risk (26, 53, and 66), and 12 as low-risk (6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81, and CP6108) (Munoz Nubia et al., 2003). In many cases even after getting infected with HPV, it is generally eliminated by the response of host’s immune system, but in many cases many cases, where HPV is not done away with by the immune system, it may develop into cervical cancer. The common risk factors linked with cervical cancer include first intercourse or pregnancy at an early age, having sex with multiple partners, weak immune system, smoking, use of oral contraceptives, improper menstrual hygiene etc. The early stages of the cervical cancer are usually asymptomatic but symptoms do appear with the progression of pre-cancer to invasive cancer and typically shows abnormal vaginal bleeding, unusual vaginal discharge, and pain during vaginal intercourse. New bleeding may be experienced by the women who have had their menopause. Cervical cancer is the second most commonly diagnosed and fifth deadliest cancer in women throughout the world. In developing countries cervical cancer has a major share in cancer mortality (Shidham et al., 2011). Every year about 5,00,000 new cases are diagnosed out of which about 2,50,000 patient die. A large majority of these cases (around 84%) are reported from the developing countries and under developed countries, as compared to the developed countries. This is attributed to mass level screening programs along with follow-ups at regular intervals done by the developed counters (Kent, 2010).

1.9.4 Papanicolaou test

The Papanicolaou test (Pap smear) has been the widely used method in cervical cancer screening for many decades and has shown a dramatic lowering of incidents of cervical cancer and hence in related mortality rates in many countries (Shidham et al., 2011). In taking a Pap smear, the cells of are scraped from the outer opening of the cervix for microscopic examination and to lookup for any unusual irregularities. The aim of the test is to detect any pre-cancerous or potentially pre-cancerous alterations called cervical intraepithelial neoplasia or cervical dysplasia. Pap test is also used to detect endo-cervix and endometrium abnormalities and infections. In many developed countries, regular

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Pap smear screening is highly recommended for females who have had frequent sex with multiple partners (Saslow et al., 2012). If any unusual findings are observed the test may need to be repeated within a year. If the abnormality observed require closer examination, a detailed cervical inspection by colposcopy may be done. HPV DNA testing may also be suggested to such patients, which acts as a supplement to Pap smear testing. Once the sample is obtained, Papanicolaou technique is used to stain it. Staining using this technique helps to differentiate the cells in smear preparation from various other bodily secretions as unstained cells cannot be seen under a simple compound microscope. Most of the abnormal results are mildly abnormal (called low-grade squamous intraepithelial lesion (LSIL)) which indicate HPV infections. Most low-grade cervical dysplasia relapse by their own without usually causing cervical cancer, but presence of dysplasia can act as a warning that a greater monitoring is needed. Generally, some of Pap results are high-grade squamous intraepithelial lesion (HSIL), and very few of them indicate cancer.

1.9.5 Bethesda System

The Bethesda system is a standard system of cytological reporting in cervicovaginal diagnosis (Apgar et al., 2003). Most popularly it is used for reporting of Pap-smear test results. It was first introduced in 1988 with an aim to standardize the terminology used and establish more consistent reports for reporting, which would facilitate clear guidelines for clinical management (Diane Soloman, 1989). Since its first publication in 1988, it was revised two times, in April 1991 and April 2001 (Nayar et al., 2004 & Solomon et al., 2002). The 2001-Bethesda system consists of several components and subcomponents, as summarized in Table 1.1
### Table 1.1 Summary of 2001-Bethesda system of reporting

<table>
<thead>
<tr>
<th>Reporting</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specimen Adequate / Inadequate</td>
<td>Specimen is considered adequate for evaluation on the basis of presence or absence of endocervical or transformation zone component and other quality indicators e.g., partially obscuring blood, inflammation, etc.</td>
</tr>
</tbody>
</table>

**Interpretation of Observations**

- **a. Negative for Intraepithelial Lesion or Malignancy**
  - **Organisms:**
    - Trichomonas vaginalis
    - Shift in flora suggestive of bacterial vaginosis
    - Bacteria morphologically consistent with Actinomyces spp
    - Fungal organisms morphologically consistent with Candida spp
    - Cellular changes consistent with herpes simplex virus
  - **Other Non-neoplastic Findings:**
    - Reactive cellular changes associated with :
      - Inflammation (includes typical repair)
      - Radiation
      - Intrauterine device (IUD)
    - Glandular cells status posthysterectomy
    - Atrophy
  - **Other:**
    - Endometrial cells (in a woman ≥ 40 years of age)

- **b. Epithelial Cell Abnormalities**
  - Squamous cell:
    - Atypical squamous cells
      - Of undetermined significance (ASC-US)
      - Cannot exclude HSIL (ASC-H)
    - Low-grade squamous intraepithelial lesion (LSIL) (encompassing: HPV/mild dysplasia/CIN1)
    - High-grade squamous intraepithelial lesion (HSIL) (encompassing: moderate and severe dysplasia, CIS, CIN 2 and CIN 3)
    - Squamous cell carcinoma
  - Glandular Cell:
    - Atypical glandular cells (AGC) (endocervical cells, endometrial cells or not otherwise specified)
    - Atypical glandular cells, favor neoplastic (endocervical cells or not otherwise specified)
  - Endocervical adenocarcinoma in situ (AIS)
  - Adenocarcinoma
  - Endometrial cells in a woman ≥ 40 years of age

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Table 1.1 Summary of 2001-Bethesda system of reporting