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# Editorial

## Contents



**Mini review section** – Mycotoxins are toxic secondary metabolites produced by fungi when they colonize the foodstuffs. These are potent toxins having severe health consequences in people, being mutagenic, teratogenic, and carcinogenic. Several fungi can produce mycotoxins on agricultural products during harvest or in postharvest, and they have significant adverse effects on both animal and human beings. The most prevalent mycotoxins found in food commodities are aflatoxins and ochratoxins produced by Aspergillus species, ochratoxins and patulin produced by Penicillium, as well as fumonisins, deoxynivalenol, and zearalenone produced by *Fusarium* species.

**Current Trends section** – One of the primary responsibilities of dental healthcare professionals is to create a safe and comfortable environment for their patients. Keeping this in view, devised protocols to prevent cross-infection among the dental patients have been developed. This involves thorough cleaning and sterilization of all types of dental instruments, each time they are used on a patient. According to the Centers for Disease Control CDC, dental instruments have been classified into three categories, depending upon their risk for transmitting infection among patients and dental healthcare providers

**In Profile Scientist** – Erwin Chargaff (1905–2002) was born in Czernowitz, which at that time was a provincial capital of the Austrian monarchy. He graduated from high school at the Maximilian Gymnasium in Vienna and went to the University of Vienna in 1923. At the university, Chargaff decided to study chemistry. Although he had never taken the subject before, it offered the most hope of employment after graduation, specifically the opportunity to work at his uncle's alcohol refinery. Unfortunately, before he even started on his dissertation, the uncle was dead and Chargaff's alcoholic hopes had evaporated. Nonetheless, he stuck with chemistry and received his doctoral degree in 1928.

**Bug of the month** – JEV is a virus from the family Flaviviridae, part of the Japanese encephalitis serocomplex of nine genetically and antigenically related viruses, some of which are particularly severe in horses, and four of which, including West Nile virus, are known to infect humans. The enveloped virus is closely related to the West Nile virus and the St. Louis encephalitis virus. The positive sense single-stranded RNA genome is packaged in the capsid which is formed by the capsid protein. The outer envelope is formed by envelope protein and is the protective antigen. It aids in entry of the virus into the cell. The genome also encodes several non-structural proteins (NS1, NS2a, NS2b, NS3, N4a, NS4b, NS5).

**Did You Know? –** Neurons in certain brain areas integrate 'what' and 'when' information to discern hidden order in events in real time. Neurons in the hippocampus help to pick out patterns in the flood of information pouring through the brain. The human brain is constantly picking up patterns in everyday experiences — and can do so without conscious thought, finds a study of neuronal activity in people who had electrodes implanted in their brain tissue for medical reasons.

**Best Practices** – For the last several years, the consumer-packaged goods (CPG) industry has been in a state of rapid, fundamental change, and today's environment has only accelerated this process. New technologies, new business models, and shifting consumer demands have transformed the market, requiring quick action and extreme flexibility from every manufacturer in the space.

Tickle yourself enjoying the jokes in our **Relax Mood** section.

Our JHS team is thankful to all our readers for their ever-increasing appreciation that has served as a reward & motivation for us. Looking forward for your continuous support.

# Fungal mycotoxins in foods: A review II

Mycotoxins are toxic secondary metabolites produced by fungi when they colonize the foodstuffs. These are potent toxins having severe health consequences in people, being mutagenic, teratogenic, and carcinogenic. Several fungi can produce mycotoxins on agricultural products during harvest or in postharvest, and they have significant adverse effects on both animal and human beings. The most prevalent mycotoxins found in food commodities are aflatoxins and ochratoxins produced by *Aspergillus* species, ochratoxins and patulin produced by *Penicillium*, as well as fumonisins, deoxynivalenol, and zearalenone produced by *Fusarium* species.

International trade in agricultural commodities such as wheat, rice, barley, corn, sorghum, soybeans, groundnuts and oilseeds amount to hundreds of millions of tonnes each year. There is a notable length of time between the purchase of the agricultural commodity at the village market of the exporting country and its arrival at the distribution centre of the importing country. The transport chain for agricultural commodities from village to port, from the port of the exporting country to that of the importing country as well as from the port to the distribution centre can be long. Furthermore, storage conditions at the farm level as well as during transport under adverse weather conditions may not always be satisfactory. For these reasons, there is considerable opportunity for mould and mycotoxin contamination of agricultural commodities to take place throughout the food system - from production to distribution and transport - and this may lead to economic losses.

**Methods of detecting mycotoxins**

Mycotoxins are toxic and poisonous, can occur even with the very small quantities in food commodities, and consumption of such food products causes several health risks. Therefore, there is a need to analysis and quantification of mycotoxins by sensitive and accurate methods. So that they can reduce before consumptions. For the quantification and detection of mycotoxins in foodstuffs, several analytical methods have been adopted.

| Methods | Advantages | Disadvantages |
|---|---|---|
| Immunoaffinity column | Good specificity and sensitivity | Costly and detect only one mycotoxin at a time |
| Solid-phase extraction | Cos-effective, more selective, long shelf life and easy in preparation | Not specific and takes longer time |
| Multifunctional columns | Long shelf life and appropriate for concurrent detection | Vulnerable to the matrix effect |
| Thin layer chromatography | Quick, simple, and qualitative method | Low sensitivity and no quantification |
| Enzyme-linked immunosorbent assay | Sample preparation easy, low-cost, and appropriate for rapid screening | Cross-reactivity and chances of false positive or negative results |
| Dual-label time-resolved fluoroimmunoassay | Good sensitivity, nonradioactive and high intensity of fluorescence | Cross-reactivity, and possible false positive or negative results |
| Multiplex flow cytometric microsphere immunoassay | No cross-interaction, suitable for simultaneous analysis of mycotoxins | Poor sensitivity and require suitable multi-mycotoxin clean-up step and specific probes |
| Immunochip | Excellent sensitivity, visual semi-quantitative, and appropriate for concurrent analysis of mycotoxins | Costly in analytical cost, complex labelling process and need professional experts |
| Immuno-rotary biosensor | Low cost, quick, accurate, and good specificity | Low stability and short useful life |
| Lateral flow immunoassay | Quick, easy, one-step, and cost-effective | Low sensitivity, and quantification negligible |
| Surface plasmon resonance | Quick speed, and no need for competition or labelled reagents | Temperature sensitive and samples components, probable false positive or negative results |
| Electronic nose | Sample handling not required, quick, preciseness, and high-flux | Low sensitivity, costly, and short useful life |
| High-performance liquid chromatography | Excellent sensitivity, repeatability, and selectivity, and suitable for concurrent multiple mycotoxins detection | Require costly equipment, and need clean-up step |
| Gas chromatography mass spectrometry | Quick, good sensitivity and repeatability | Require costly equipment, derivatization and clean-up step |
| Liquid chromatography tandem mass spectrometry | Good sensitivity, repeatability, and reproducibility, appropriate for concurrent analysis of mycotoxins and derivatization not required | Costley equipment, samples require clean-up step, and matrix effects |

**Prevention and control of mycotoxins in foods**

Several preventive measures to minimize mycotoxin contamination in agricultural commodities have been attempted. These can be divided into three broad categories:

- plant breeding.
- good agronomic practices.
- detoxification.

The problem of ergot contamination of cereals and millets has been successfully minimized in the past by cultivating varieties of rye, wheat and pearl millet that are resistant to the disease. Following good agricultural practices during both pre-harvest and post-harvest conditions would, minimize the problem of contamination by mycotoxins such as aflatoxins, ochratoxin and trichothecene mycotoxins. These include appropriate drying

techniques, maintaining proper storage facilities and taking care not to expose the grains or oilseeds to moisture during transport and marketing. The method of segregating contaminated, mouldy, shrivelled or insect-infested seeds from sound kernels has been particularly useful in minimizing aflatoxin contamination in peanuts.

Mycotoxin control measures have been implemented for agricultural commodities entering international trade or located in countries with centralized or large-scale buying and distribution systems.

**Removal of mycotoxins in foods**

In the feed and food industry it has become common practice to add mycotoxin binding agents such as montmorillonite or bentonite clay in order to affectively adsorb the mycotoxins. To reverse the adverse effects of mycotoxins, the following criteria are used to evaluate the functionality of any binding additive:

- Efficacy of active component verified by scientific data.
- A low effective inclusion rate.
- Stability over a wide pH range.
- High capacity to absorb high concentrations of mycotoxins.
- High affinity to absorb low concentrations of mycotoxins.
- Affirmation of chemical interaction between mycotoxin and adsorbent.
- Proven *in vivo* data with all major mycotoxins.
- Non-toxic, environmentally friendly component.

Since not all mycotoxins can be bound to such agents, the latest approach to mycotoxin control is mycotoxin deactivation. By means of enzymes (esterase, de-epoxidase), yeast (*Trichosporon mycotoxinvorans*), or bacterial strains (Eubacterium BBSH 797), mycotoxins can be reduced during pre-harvesting contamination. Other removal methods include physical separation, washing, milling, nixtamalization, heat-treatment, radiation, extraction with solvents, and the use of chemical or biological agents. Irradiation methods have proven to be effective treatment against mold growth and toxin production.

**Regulations on mycotoxins in foods**

Many international agencies are trying to achieve universal standardization of regulatory limits for mycotoxins. The process of assessing a need for mycotoxin regulation includes a wide array of in-laboratory testing that includes extracting, clean-up and separation techniques. Most official regulations and control methods are based on high-performance liquid techniques through international bodies. It is implied that any regulations regarding these toxins will be in co- ordinance with any other countries with which a trade agreement exists. It is through various compliance programs that the FDA monitors these industries to guarantee that mycotoxins are kept at a practical level. These compliance programs sample food products including peanuts and peanut products, tree nuts, corn and corn products, cottonseed, and milk. Mycotoxins have been widely studied and their implications in foods are enormous. Regulatory control and fast and effective analyses and detection will go a long way in reducing the danger of mycotoxins in foods.

# Sterilization and Disinfection Methods in Dentistry

One of the primary responsibilities of dental healthcare professionals is to create a safe and comfortable environment for their patients. Keeping this in view, devised protocols to prevent cross-infection among the dental patients have been developed. This involves thorough cleaning and sterilization of all types of dental instruments, each time they are used on a patient.

According to the Centers for Disease Control CDC, dental instruments have been classified into three categories, depending upon their risk for transmitting infection among patients and dental healthcare providers:

**1. Critical Instruments:**
These include all instruments that penetrate oral soft tissues and bone or are exposed to the bloodstream. These instruments should be sterilized through heat, dry or chemical sterilization, after each use, Critical instruments used in dentistry include dental forceps, scalpels, bone chisels and surgical burs.

**2. Semi-critical Instruments:**
These instruments do not penetrate oral tissues. However, they encounter oral mucous membrane or non-intact skin. Such instruments include dental mirrors, amalgam condensers and impression trays. The CDC recommends that these instruments should ideally be sterilized after each use.

**3. Non-critical Instruments:**
These instruments only encounter the intact skin or mucous membrane. Such instruments include x-ray heads and pulse oximeters. These instruments have a low risk of cross-infection. Therefore, they can be cleaned with an intermediate or low-level disinfectant.

Processing of Dental Instruments Before and After Sterilization
Sterilization or disinfection of dental instruments is only effective, if it is performed properly. Here are a few things that must be kept in mind by dental professionals who are involved in sterilization of dental instruments:

**• Designate a Separate Instrument Washing Area:**
Contaminated dental instruments need to be cleaned of blood and debris before sterilization. Each dental practice should create a separate place that is reserved for cleaning of contaminated dental instruments. Care should be taken to immerse the instruments into water or detergent immediately after use, to prevent drying of blood and debris. Dental professional should wear heavy gloves while washing instruments, to prevent accidental injury and cross-infection. Ultrasonic machines can also be used for improved cleaning.

**• Packaging and Storage of Instruments:**
Instruments that are to be used in a specific procedure, are placed in special packages before sterilization. In this way, there are minimal chances of contamination of the instruments during storage and transport, once they have been sterilized. Alternatively, sterilization cassettes can also be used to sterilize a set of instruments that are required during a specific dental procedure. These cassettes allow easier arrangement of dental instruments, and reduce chances of injury and damage during cleaning, packaging, and storage.

**The Sterilization Procedure**
Different methods of sterilization are used in dentistry, based on required depth of sterilization as well as the type of dental material:

**1. Sterilization Using Steam Autoclave**
This is the most effective and most used method of sterilization in dental practices. This is because pressurized steam in an autoclave can get rid of all types of microbes and their spores. Instruments in an autoclave are sterilized at 121° C for 15 minutes and 15 pounds pressure.

**2. Dry Heat Ovens**
These are electrical devices, which use dry heat to sterilize dental instruments. Since they do not require water for sterilization, much pressure is not developed inside them. Therefore, they are safer than the steam autoclaves. Since heat generation is electrically controlled, optimal temperatures for sterilization are rapidly attained. However, dry heat ovens may not be able to completely kill all microbes such as prions. Dry heat ovens are used to sterilize those instruments which do not get burnt during heating, such as glass slabs or powders.

**3. Chemical Vapor Sterilization**

During chemical vapor sterilization, a mixture of various chemicals such as alcohol, ketones, formaldehyde, and water are heated under pressure to form a sterilization gas. Typical sterilization procedure requires 20 minutes at 270°F, under 20 psi pressure to completed.

**4. Cold Sterilization**

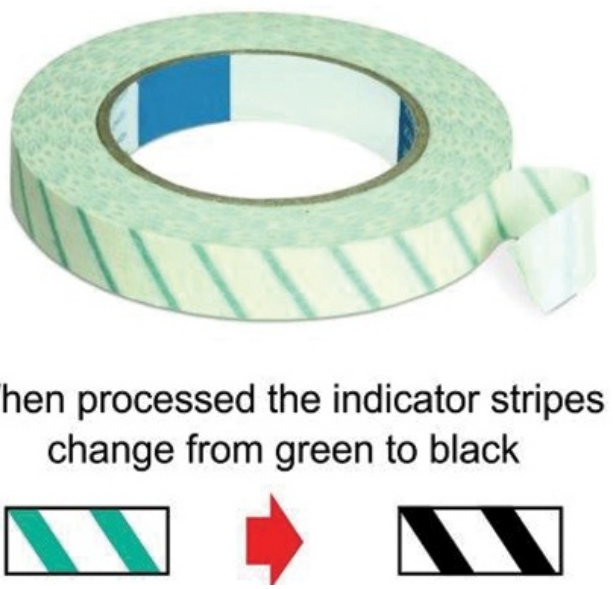
This type of sterilization is used on heat-sensitive dental instruments. Solutions such as glutaraldehyde or Sodium hypochlorite may be used for this purpose. However, this procedure requires a lot of time to acquire complete sterilization, and therefore it is not recommended. These chemicals can, however, be used for high level disinfection purposes.

**How to Ensure Effective Sterilization:**

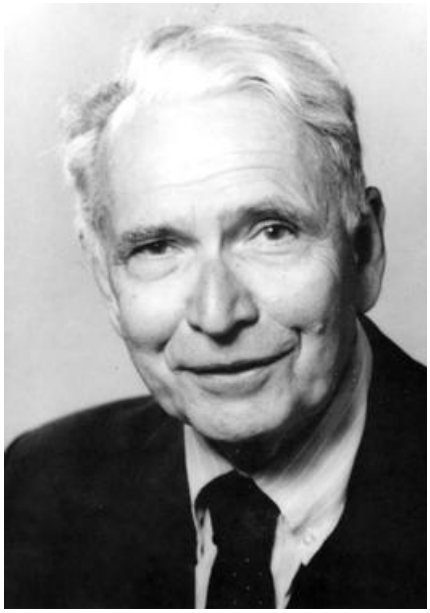
Complete sterilization of dental instruments is imperative in obtaining perfect cross-infection protocol. Therefore, the use of various indicators to make sure that complete sterilization has taken place comes in aid.

• **Biological Indicators** – this type of sterilization test involves the use of highly resistant bacterial spores such as *Bacillus stearothermophilus* (used as indicator for steam and chemical sterilization), or *Bacillus subtilis* (for monitoring dry heat sterilization).

• **Chemical Indicators** – these are heat sensitive indicators, which change colour upon exposure to heat or steam. They are used in the form of tapes or strips and are attached to the instrument packages to monitor sterilization. In case of unwrapped instruments, they are also placed in difficult-to-reach areas, to assess the level of sterilization. It is the professional obligation of dentists to provide a safe and comfortable environment for their patients. Therefore, all dental practices should devise and implement an effective sterilization and cross-infection protocol, for the safety of the patients as well as the dental team.



## Erwin Chargaff



Erwin Chargaff (1905–2002) was born in Czernowitz, which at that time was a provincial capital of the Austrian monarchy. He graduated from high school at the Maximilian Gymnasium in Vienna and went to the University of Vienna in 1923. At the university, Chargaff decided to study chemistry. Although he had never taken the subject before, it offered the most hope of employment after graduation, specifically the opportunity to work at his uncle's alcohol refinery. Unfortunately, before he even started on his dissertation, the uncle was dead and Chargaff's alcoholic hopes had evaporated. Nonetheless, he stuck with chemistry and received his doctoral degree in 1928. His dissertation, done under the supervision of Fritz Feigl, dealt with organic silver complexes and with the action of iodine on azides. Because there were very few research positions in Austria, Chargaff left for the United States in 1928 as a Milton Campbell Research Fellow at Yale University. He found America agreeable enough that he remained there for two years, working with R. J. Anderson on tubercle bacilli and other acid-fast microorganisms.

In the summer of 1930, Chargaff returned to Europe and was appointed Assistent at the Bacteriology Department of the University of Berlin. His work in Berlin covered a variety of topics including a study of the lipids of the bacillus Calmette-Gue´rin and a detailed investigation of the fat and phosphatide fractions of diphtheria bacteria. However, with the rise of Hitler, Chargaff felt the need to leave Germany, and in 1933 he transferred to the Pasteur Institute in Paris. During his brief time in Paris, he worked on bacterial pigments and polysaccharides. Then, in 1935 he returned to the United States to become an assistant professor of biochemistry at Columbia University. Seventeen years later he became a full professor and later was chairman of the department from 1970 to 1974, when he retired to emeritus status.

In 1944, Chargaff read Oswald Avery's report that the hereditary units, the genes, were composed of DNA. This had a profound impact on Chargaff. Thus started Chargaff's work on the chemistry of nucleic acids. He began with the belief that if DNA from different species exhibited different biological activities, there should also be chemically demonstrable differences between the DNA. His immediate challenge was to devise a method to analyze the nitrogenous components and sugars of DNA from different species. Because large amounts of DNA would be hard to come by, his methods also had to be applicable to small amounts of material. The formulation of this procedure took two years and was aided by several recent technological developments including the introduction of paper chromatography to separate and identify minute quantities of organic substances and the photoelectric ultraviolet spectrophotometer. His procedure consisted of three steps. The first was the separation of the DNA mixture into individual components by paper chromatography. Next, the separated compounds were converted into mercury salts. And finally, the purines and pyrimidines were identified via their ultraviolet absorption spectra. Chargaff tested the method on several mixtures of purines and pyrimidines and reported his encouraging results in the Classic. In a separate paper, printed back-to-back with the Classic, he put his method to use and analyzed the DNA composition of yeast and pancreatic cells. A month later, Chargaff submitted two additional papers to the JBC on the complete qualitative analysis of several DNA preparations. The first paper dealt with the purines and pyrimidines of the DNA of calf thymus and beef spleen and the second with the DNA of tubercle bacilli and yeast. Although these papers would eventually prove to be invaluable contributions to our understanding of the structure of DNA and the genetic code, they were almost not published. "One curious circumstance attending the publication of these papers deserves mention because it illustrates the ignorance about nucleic acids that then prevailed among the scientific elite," wrote Chargaff. "I had, at that time, already published something like 75 articles in the Journal of Biological Chemistry without ever having one sent back by the editor for clarification or revision. The papers about DNA composition, however, were returned to me with a particularly silly objection. How could I, the editor asked, express the composition of a DNA as moles of adenine or guanine, cytosine or thymine, per gram-atom of phosphorus, since the purines and pyrimidines did not contain any phosphorus? After I had repeated, in my answer to the editor, part of the introductory lecture on the nucleic acids, which at that time I was already giving to the first-year medical students at Columbia, we achieved grudging reconciliation". Over time, Chargaff improved on his initial quantification methods by introducing formic acid hydrolysis for the simultaneous liberation of all nitrogenous constituents and by using a UV lamp to demonstrate the separated adsorption zones on the filter strip. These improvements permitted him to rapidly analyze DNA from a variety of species.

Eventually, Chargaff summarized his findings on the chemistry of nucleic acids in a review in 1950. His two main discoveries, (i) that in any double-stranded DNA the number of guanine units equals the number of cytosine units and the number of adenine units equals the number of thymine units and (ii) that the composition of DNA varies from one species to another, are Erwin Chargaff. These results provided the firm evidence needed to disprove the prevailing tetranucleotide hypothesis. The hypothesis, originally put forth by JBC Classic author Phoebus Levene, stated that DNA was composed of a large number of repeats of a GACT tetramer, which was obviously no longer valid. Chargaff's research also helped lay the groundwork for James Watson and Francis Crick's discovery of the double-helix structure of DNA.

# Jokes

Teacher: "Kids, what does the chicken give you?"

Student: "Meat!"

Teacher: "Very good! Now what does the pig give you?"

Student: "Bacon!"

Teacher: "Great! And what does the fat cow give you?"

Student: "Homework!"

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A teacher asked her students to use the word "beans" in a sentence.

"My father grows beans," said one girl.

"My mother cooks beans," said a boy.

A third student spoke up, "We are all human beans."

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A boy asks his father, "Dad, are bugs good to eat?"

"That's disgusting. Don't talk about things like that over dinner," the dad replies.

After dinner the father asks, "Now, son, what did you want to ask me?"

"Oh, nothing," the boy says. "There was a bug in your soup, but now it's gone."

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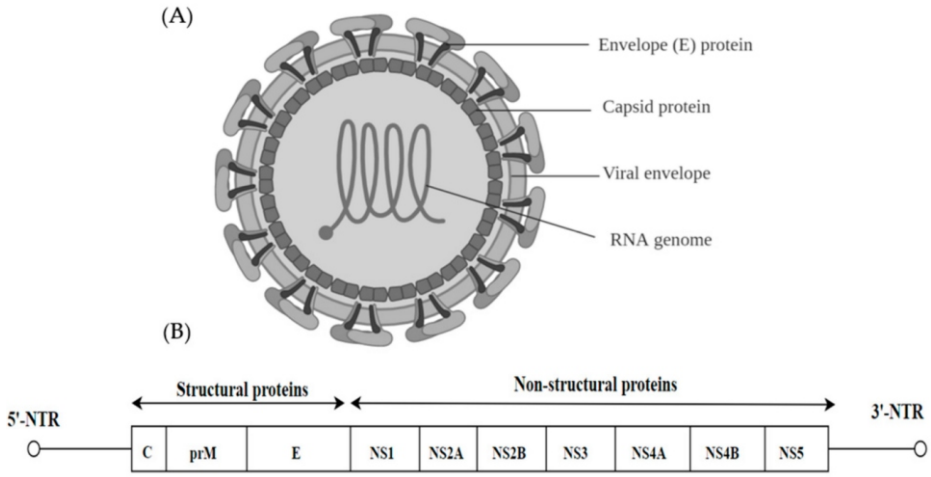
A mom texts, "Hi! Son, what does IDK, LY, & TTYL mean?"

He texts back, "I Don't Know, Love You, & Talk To You Later."

The mom texts him, "It's ok, don't worry about it. I'll ask your sister, love you too."

# Japanese encephalitis Virus




JEV is a virus from the family *Flaviviridae*, part of the *Japanese encephalitis serocomplex* of nine genetically and antigenically related viruses, some of which are particularly severe in horses, and four of which, including West Nile virus, are known to infect humans. The enveloped virus is closely related to the West Nile virus and the St. Louis encephalitis virus. The positive sense single-stranded RNA genome is packaged in the capsid which is formed by the capsid protein. The outer envelope is formed by envelope protein and is the protective antigen. It aids in entry of the virus into the cell. The genome also encodes several non-structural proteins (NS1, NS2a, NS2b, NS3, N4a, NS4b, NS5). NS1 is produced as a secretory form also. NS3 is a putative helicase, and NS5 is the viral polymerase. It has been noted that Japanese encephalitis infects the lumen of the endoplasmic reticulum (ER) and rapidly accumulates substantial amounts of viral proteins.

Based on the envelope gene, there are five genotypes (I–V). The Muar strain, isolated from a patient in Malaya in 1952, is the prototype strain of genotype V. Genotype V is the earliest recognized ancestral strain. The first clinical reports date from 1870, but the virus appears to have evolved in the mid-16th century. Complete genomes 372 strains of this virus have been sequenced as of 2024.

Japanese encephalitis (JE) is an infection of the brain caused by the Japanese encephalitis virus (JEV). While most infections result in little or no symptoms, occasional inflammation of the brain occurs. In these cases, symptoms may include headache, vomiting, fever, confusion and seizures. This occurs about 5 to 15 days after infection. JEV is generally spread by mosquitoes, specifically those of the *Culex* type. Pigs and wild birds serve as a reservoir for the virus. The disease occurs mostly outside of cities. Diagnosis is based on blood or cerebrospinal fluid testing.

Prevention is generally achieved with the Japanese encephalitis vaccine, which is both safe and effective. Other measures include avoiding mosquito bites. Once infected, there is no specific treatment, with care being supportive. This is generally carried out in a hospital. Permanent problems occur in up to half of people who recover from JE.

The Japanese encephalitis virus (JEV) has an incubation period of 2 to 26 days. The vast majority of infections are asymptomatic: only 1 in 250 infections develop into encephalitis. Severe rigors may mark the onset of this disease in humans. Fever, headache and malaise are other non-specific symptoms of this disease which may last for a period of between 1 and 6 days. Signs which develop during the acute encephalitic stage include neck rigidity, cachexia, hemiparesis, convulsions and a raised body temperature between 38–41 °C (100.4–105.8 °F). The mortality rate of the disease is around 25% and is generally higher in children under five, the immuno-suppressed and the elderly. Transplacental spread has been noted. Neurological disorders develop in 40% of those who survive with lifelong neurological defects such as deafness, emotional lability and hemiparesis occurring in those who had central nervous system involvement.

Japanese encephalitis virus enters the brain through two ways and leads to infection of neurons and encephalitis.Increased microglial activation following Japanese encephalitis infection has been found to influence the outcome of viral pathogenesis. Microglia are the resident immune cells of the central nervous system (CNS) and have a critical role in host defense against invading microorganisms. Activated microglia secrete cytokines, such as interleukin-1 (IL-1) and tumor necrosis factor alpha (TNF-α), which can cause toxic effects in the brain. Additionally, other soluble factors such as neurotoxins, excitatory neurotransmitters, prostaglandin, reactive oxygen, and nitrogen species are secreted by activated microglia.

In a murine model of JE, it was found that in the hippocampus and the striatum, the number of activated microglia was more than anywhere else in the brain, closely followed by that in the thalamus. In the cortex, the number of activated microglia was significantly less when compared to other regions of the mouse brain. An overall induction of differential expression of proinflammatory cytokines and chemokines from different brain

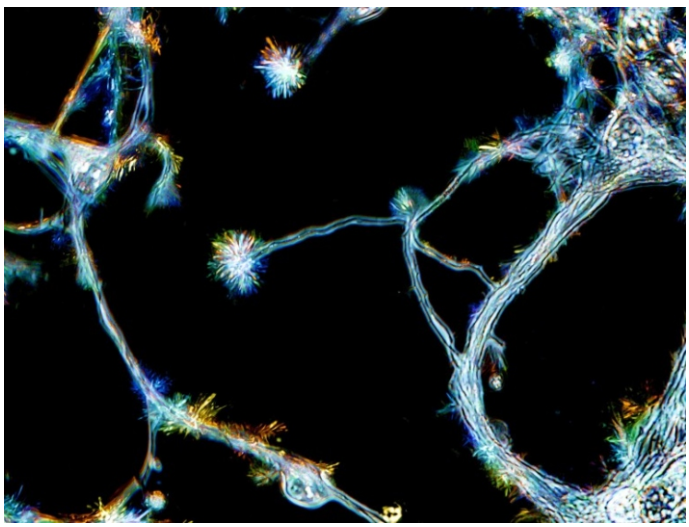
regions during a progressive Japanese encephalitis infection was also observed. Although the net effect of the proinflammatory mediators is to kill infectious organisms and infected cells as well as to stimulate the production of molecules that amplify the mounting response to damage, it is also evident that in a non regenerating organ such as the brain, a dysregulated innate immune response would be deleterious. In JE the tight regulation of microglial activation appears to be disturbed, resulting in an autotoxic loop of microglial activation that possibly leads to bystander neuronal damage. In animals, key signs include infertility and abortion in pigs, neurological disease in horses, and systemic signs including fever, lethargy and anorexia.

Japanese encephalitis is diagnosed by commercially available tests detecting JE virus-specific IgM antibodies in serum and/or cerebrospinal fluid, for example by IgM capture ELISA. There is no specific treatment for Japanese encephalitis and treatment is supportive, with assistance given for feeding, breathing or seizure control as required. Raised intracranial pressure may be managed with mannitol. There is no transmission from person to person and therefore patients do not need to be isolated.

A breakthrough in the field of Japanese encephalitis therapeutics is the identification of macrophage receptor involvement in the disease severity. A recent report of an Indian group demonstrates the involvement of monocyte and macrophage receptor CLEC5A in severe inflammatory response in Japanese encephalitis infection of the brain. This transcriptomic study provides a hypothesis of neuroinflammation and a new lead in development of appropriate therapies for Japanese encephalitis. The effectiveness of intravenous immunoglobulin for the management of encephalitis is unclear due to a lack of evidence. Intravenous immunoglobulin for Japanese encephalitis appeared to have no benefit.

Infection with Japanese encephalitis confers lifelong immunity. There are currently three vaccines available: SA14-14-2, IXIARO (IC51, also marketed in Australia, New Zealand as JESPECT and India as JEEV) and ChimeriVax-JE (marketed as IMOJEV). All current vaccines are based on the genotype III virus.

# How your brain detects patterns in the everyday: without conscious thought



Neurons in certain brain areas integrate 'what' and 'when' information to discern hidden order in events in real time.

Neurons in the hippocampus help to pick out patterns in the flood of information pouring through the brain.

The human brain is constantly picking up patterns in everyday experiences — and can do so without conscious thought, finds a study of neuronal activity in people who had electrodes implanted in their brain tissue for medical reasons.

The study shows that neurons in key brain regions combine information on what occurs and when, allowing the brain to pick out the patterns in events as they unfold over time. That helps the brain to predict coming events, the authors say. The work was published today in Nature.

"The brain does a lot of things that we are not consciously aware of," says Edvard Moser, a neuroscientist at the Norwegian University of Science and Technology in Trondheim. "This is no exception."

**Blizzard of data**

To make sense of the world around us, the brain must process an onslaught of information on what happens, where it happens and when it happens. The study's authors wanted to explore how the brain organizes this information over time — a crucial step in learning and memory.

The team studied 17 people who had epilepsy and had electrodes implanted in their brains in preparation for surgical treatment. These electrodes allowed the authors to directly capture the activity of individual neurons in multiple brain regions.

Among those regions were the hippocampus and entorhinal cortex, which are involved in memory and navigation. These areas contain time and place cells that act as the body's internal clock and GPS system, encoding time and locations. "All the external world coming into our brain has to be filtered through that system," says study co-author Itzhak Fried, a neurosurgeon and neuroscientist at the University of California, Los Angeles.

**Parade of faces**

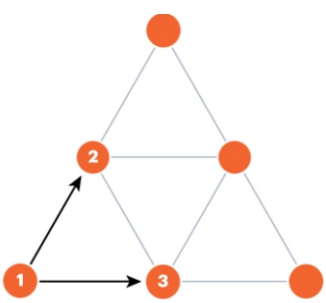
In preparation for the main experiment, the researchers showed each participant a variety of images of faces. For each participant, the scientists identified six of the faces that prompted an individual neuron in the participant's brain to fire strongly. A participant might have a 'man in sunglasses' neuron, for example, along with a 'woman in a hat' neuron and four more that each favoured a particular face.

The team arranged each participant's six images in a triangle that had one image at each corner and one on each side. Each image was connected to its nearest neighbours by lines running down the triangle's sides and through its interior.

In an experimental trial, participants viewed a series of the face images. A simple rule dictated the sequence of images: each face was followed by one that was connected to it on the triangle (see 'Pattern recognition'). For example, if the first face was the one on the triangle's bottom left corner, the second face would be one of its two direct neighbours: the face in the middle of the triangle's base or the face in the middle of the triangle's left side. The experimenters did not reveal this rule to participants. What's more, they distracted the participants by asking them questions about the images' content during each trial.

**PATTERN RECOGNITION**

Researchers arranged pictures of six faces on a triangle, placing one at each of the circles. Study participants were shown the pictures in sequence, with every picture followed by one of its neighbours. For example, if the first picture a participant saw was the face at position 1, the second picture would be the face at either position 2 or position 3.




During the experiment, neurons in each participant's hippocampus and entorhinal cortex gradually began to respond not only to the face being presented but also to faces directly connected to it on the triangle. When asked whether they noticed any pattern in the order of the images, the participants said they didn't. But their brain cells still learnt the pattern, showing that the brain can recognize patterns without conscious awareness. In the breaks between trials, the participants' 'face' neurons replayed what they had learnt, cycling through the patterns on their own without being stimulated to do so.

"This is something that is not explicit, it is implicit. And the brain gets it, essentially, very quickly, and we can see those changes in the individual cells," says Fried.

**Future-facing neurons**

The authors found that the neurons could also anticipate what images would appear next, suggesting that the brain can learn to predict future events on the basis of learnt patterns.

"The fact that's happening without any external motivator is really interesting," says Matt Jones, a neuroscientist at the University of Bristol, UK. "Many of the findings are remarkably consistent with predictions from rodent work, highlighting how hippocampal circuits have evolved to structure our cognitive maps," he adds.

Understanding how the brain organizes information about sequences of events could have important clinical applications. For example, memory-enhancement therapies might focus on boosting specific neuronal patterns that represent important memories, says Fried. "It's eventually a question of putting things together in time. This is really the crux of memory."

# Best Practices to Drive Your Competitive Edge in CPG Manufacturing

For the last several years, the consumer-packaged goods (CPG) industry has been in a state of rapid, fundamental change, and today's environment has only accelerated this process. New technologies, new business models, and shifting consumer demands have transformed the market, requiring quick action and extreme flexibility from every manufacturer in the space.

How can manufacturers prosper in this time of transition? The top ten best practices for keeping progressive CPGs ahead of the curve were determined based on the results.

**1. Deploy mixed mode manufacturing to gain competitive advantage**

Roughly 44% of the CPG manufacturers surveyed are abandoning the traditional division between manufacturing to gain discrete and process manufacturing in favour of mixed mode systems. By combining both processes into the same plant—or even applying them to the same product—using a shared cloud-based software backbone, mixed-mode manufacturing has allowed CPG businesses to increase flexibility and responsiveness, earn greater distribution and market share, and, above all, grow revenue.

**2.Outpace change with real-time data and visibility across your supply chain**

Not surprisingly, 80% of CPG manufacturers agree that access to data is either "critical" or "very important" to their decision-making process. But to truly thrive in this data-driven era, CPG manufacturers need to develop a seamless, end-to-end data trail throughout the entire manufacturing and delivery process. This data, when collected through a cloud application, provides the insight needed to improve production, identify supply or operational issues, and deliver the highest quality products. It also provides a "single point of truth" and complete visibility of status and operations across the multitude of historically disconnected systems that stretch from design to manufacturing to the hands of the customer.

**3.Optimize business operations with smart manufacturing**

Many CPG manufacturers are on a clear path toward smart manufacturing: a true digital transformation that pulls data from across the enterprise into operations. In total, 40% currently have an enterprise-wide strategic roadmap to drive this, but 51% of cloud users are already following such a plan, nearly twice that of on-premises users. Cloud users hold a distinct advantage in these efforts because they have a structured approach to exploring the tools, technologies, and strategies of smart manufacturing. This makes them far more likely to drive process automation and align operations to real-time fluctuations in customer demand.

**4. Increase productivity and lower costs with predictive maintenance**

CPG manufacturers using cloud applications are 158% more likely to have "excellent" predictive maintenance processes than their on-premises competitors. By pulling in real-time data from the full breadth of machines, processes, and manufacturing systems, artificial intelligence-driven analytics can detect otherwise undetectable variations in performance and automatically schedule maintenance to stop downtime before it occurs.This is the single most powerful tool in the smart manufacturing arsenal to cut costs and improve productivity.

**5. Advance customer centricity with cloud applications**

Nearly 60% of survey respondents indicate that they are either already using cloud technologies or have plans to migrate their key applications—and another 20% are already using cloud/on-premises hybrid solutions in their operations. Leveraging cloud has proven critical to market leaders, providing the flexibility needed to meet today's extreme market dynamics, plus the capability to pull together key data from consumers as well as across the manufacturing and supply chain ecosystems. These features are essential to accelerating innovation and producing new products faster to exceed customer expectations.

**6. Anticipate and respond quickly to changing customer demand by connecting your ecosystem**

Cloud users are over 63% more likely to be developing full ecosystem collaboration than on-premises competitors. By leveraging cloud to connect not only their own enterprises and distribution chains but their entire manufacturing ecosystems—from contract manufacturers and suppliers to retailers and wholesalers—CPG leaders can clearly identify sales trends before the market, anticipate supply issues before they delay production, and align manufacturing to customer needs. This allows them to respond faster and serve customers better than the competition.

**7. Leverage pre-built solutions with embedded emerging technologies**

Survey respondents identify a host of emerging technologies they are currently or considering leveraging in their operations. Top choices include predictive analytics at 58% and artificial intelligence/machine learning at 51%—all beating the far more established IoT at just 44%. This signals that technology innovation is becoming a core competitive differentiator. For some, implementation complexities can stop digital progress before it begins. Savvy CPG manufacturers can bypass this roadblock by embracing cloud applications pre-built with embedded emerging technologies. These applications are scalable to business requirements and present a perfect opportunity to get a head start on modernizing critical operations systems.

**8. Outperform competitors with (artificial) intelligence**

Of the 51% of CPG manufacturers working toward artificial intelligence (AI) and machine learning, 26% are already leveraging the technology and another 25% are considering doing so. This result isn't entirely surprising. Coping with vast

amounts of enterprise data, consumer data, partner data, and data generated from sensors and IoT applications can become incredibly challenging. By tapping into big data streams, artificial intelligence and machine learning transform data into valuable insights by detecting patterns, trends, and irregularities—from deliveries to quality specs to orders to returns.

**9. Improve transparency and trust with track and trace capabilities**

Nearly a quarter of survey respondents are looking at the next big technological advancement to help improve their track and trace capabilities: blockchain. In fact, early adopters are already seeing powerful benefits.

By providing an uneditable log of each step of the manufacturing and delivery process, blockchain creates an unprecedented bond of trust between the producer and the consumer. For the CPG industry, this reduces the need for intermediaries between producers and consumers, shifting power from retailers to consumers. To further customer centricity, CPG companies are exploring how blockchain can facilitate direct to consumer opportunities.

**10. Don't get left behind: Act now**

The CPG industry has reached an inflection point. With expanding markets, wild demand volatility, and an environment of extreme change, only the nimble and resilient will succeed.

Thriving in this ever-evolving environment depends heavily on the ability to understand obstacles, assess expectations, and effectively harness modern technologies. Every manufacturer must begin that journey today or risk getting left behind.

## Highlights of the coming issue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Contents

**Mini Review**
Antibiotics versus biofilm: an emerging battleground in microbial communities.

**Current Trends**
Equipment Sterilization Disinfection.

**In Profile**
Alexander Fleming.

**Bug of the Month**
Oropouche virus.

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