TWO Monash medical researchers have discovered that a chemical called 5,6-DHT attacks and rapidly destroys bowel cancer cells in laboratory rats.

Their experiments show that it acts within an hour of being injected beneath the peritoneum, the membrane lining the abdominal wall.

After 48 hours, a single dose causes varying amounts of damage to tumors, killing anything from 20 per cent to more than 90 per cent of malignant cells.

And unlike radiation therapy and anti-cancer drugs now used to treat human cancers, 5,6-DHT does not harm surrounding healthy tissue or the body's natural immune system.

Synthetic hormone

The chemical is a toxic, synthetic substance but is a close relative to a naturally-occurring hormone called serotinin which is found in various parts of the body including the brain, gut, and blood cells.

Its cancer-killing abilities were discovered by Dr. Peter Tutton and Dr. David Barkla of the University's anatomy department. Tutton is a specialist in the study of cell proliferation and Barkla is an expert in the study of cells by electron microscopy.

They have been working together on cancer research for more than two years, partly by a new Bladin Fellowship awarded to them by the Anti-Cancer Council. The Fellowship recognises the contributions of Melbourne company director Mr. Fred Bladin to the financing of cancer research.

A scientific paper describing their findings has been accepted for priority publication this month by the prestigious American journal "Cancer Research".

While being cautious about the possible ramifications of their research, Tutton and Barkla feel the results achieved in rats with 5.6-DHT are impressive compared with those of anti-cancer drugs now being used therapeutically.

The researchers warn, however, that much more research and experimentation is needed before 5,6-DHT could be considered for use in humans.

"Whether it is as effective against other types of tumor, and in animals other than rats, has still to be proved," Tutton explains.

"And because it has never before been considered as a therapeutic drug, it will need to be thoroughly tested for possible side effects."

Cancer of the colon is one of the more common forms of cancer in western countries. According to the statistics of the Anti-Cancer Council of Victoria, it affects about one in 40 Australian females and one in 50 males.

"It seems to affect in many ways the ability of the cancer cell to maintain itself, such as by pumping out unwanted substances that have leaked in and pumping in nutritional substances needed to maintain its volume and to enable it to spread by continually dividing," says Tutton.

The general effect, in most cases, is...
How to save a pile on building costs...

CONSTRUCTION costs of elevated freeways and high-rise buildings could be cut by anything from 10 to 25 per cent as a result of research findings by a Monash engineering team studying foundation construction methods.

They have discovered that most foundations based on soft "bedrock" are made deeper than necessary—an ultra-conservative design approach adopted because of a previous lack of data on the material’s load-carrying capacity.

"The attitude has correctly been to go for safety at the expense of economy," says lecturer Dr. Ian Johnston, a senior member of the team.

The Victorian State Government’s Country Roads Board, which has backed part of the Monash project with technical and financial assistance, has already made use of the initial findings. It has redesigned the foundations of a major inner city bridge now under construction.

Chemical kills cancer cells

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to make affected tumors first become inflamed and swollen and then rapidly shrink into a shapeless mass of dead cells—all within 48 hours.

"Two things puzzle us about the initial experiment," says Tutton: "First we don’t know yet how or why it works; that is, just how it attacks the mitochondria. And secondly, in the 48-hour observation period of the experiment, it worked better against some tumors than others."

In rats with more than one tumor it destroyed 80-90 per cent of the cells in some and only 20 per cent in others.

Whether or not more than one injection of 5,6-DHT over a longer period than 48 hours would give a complete kill of all cancerous cells in all tumors is just one of the things to be determined in future experimentation.

Tutton and Barkla point out, however, that anti-cancer agents at present in use against some human cancers, notably leukaemia, are not expected to destroy all tumor cells. Therapy is based on using them to reduce the number of malignant cells to a point where the body’s natural immune system can overpower the remainder.

The two researchers tested the 5,6-DHT on 13 male rats which for 20 weeks were given injections of a substance known to cause colon cancer in rats and mice.

The rodents were then given the single injection of 5,6-DHT and killed at intervals of one, two, six, 16 and 48 hours. Specimens of healthy and cancerous tissue from their colons were examined with the unaided eye and by both light and electron microscopy.

"Control" animals injected with the tumor-inducing drug but not subsequently treated with 5,6-DHT were also killed and examined. These showed "moderately well-differentiated adenocarcinomas (glandular cancers) closely resembling human colorectal (lower bowel) tumors," the scientists report.

Blood pressure

After injection with 5,6-DHT the 13 experimental rats became blanched in appearance and somewhat lethargic—predictable symptoms because the substance is known to cause high blood pressure.

The symptoms were less evident in eight of the rats which were also injected with Phenotolamine, a drug which acts against high blood pressure.

One rat treated with 5,6-DHT but not Phenotolamine died from a stroke as a result of high blood pressure and was not included in the study. The other 12 displayed the symptoms of high blood pressure for a short time, after which these disappeared. The scientists then observed these reactions:

- **Many colonic tumors** in the surviving rats, when examined one, two, six and 16 hours after 5,6-DHT treatment, were hyperaemic (full of blood) in appearance and showed areas of surface bleeding.

Tumors examined 48 hours after treatment were usually a pale grey "dead meat" color. But healthy surrounding cells retained their normal appearance, except in one animal which showed a tiny, brown-colored area around one tumor.

- **Under a light microscope**, tumor sections taken one and two hours after 5,6-DHT treatment showed dilated blood vessels and increased numbers of leucocytes (white blood cells).

"At six hours following treatment, light microscopy of sections of tumor showed areas of dead and degenerating cells. A common characteristic observed was a distorted shape.

"Sections of specimens taken 16 hours after treatment showed widespread destruction of malignant cells," the researchers say.

However, not all of the tumor mass was equally affected and some glandular formations remained evident in the majority of cases.
testing and analysis of mudstone samples, and from its consulting work on a number of major projects. It has produced at least 20 consultancy reports and technical papers on the subject.

Melbourne mudstone forms a major part of the geology of the metropolitan area. To the east of the city the mudstone is close to the surface. To the west and south of the city centre it lies to a depth up to 50 metres in places—before the mudstone is reached, with perhaps a further 10 metres of drilling to form the rock socket.

Because of the variety of constructions using rock-socketed piles, it is not possible to specify a general percentage saving in building costs. Foundations are generally a fairly low proportion of the cost of buildings with high superstructures. But savings for high-rise buildings might be in the order of 10 per cent overall, says Johnston.

Where, however, the foundation component is high in proportion to the superstructure, as in the case of elevated sections of freeways, the saving could be as high as 25 per cent.

Quoting the case of the F9 Freeway, Williams said that because 45 metres of alluvium would have to be penetrated before the mudstone was reached, it would be necessary to use 100-200 high-load capacity piles with a diameter of 100 mm to about two metres. Williams has been working on tests of the load-bearing capacity of small diameter piles on the Mulgrave Freeway construction site, where the mudstone is conveniently exposed.

In the near future, at a suburban brick pit which is another conveniently exposed site, he will load larger diameter piles to failure, then investigate just how they fail.

An important aspect of this phase of the research will be the measurement of the load borne by the sides of the pile. Some design regulations have, until now, been based on the premise that the main load is borne by the base of the pile, and data have not been available to convince authorities otherwise.

Williams says that tests made at the Johnson Street Bridge site in South Melbourne indicated that 80 per cent of the load was being taken by the sides of the piles.

In support of the view that present design methods are over-conservative, Williams says that a test pile at the Johnson Street site was loaded to 1300 tons—twice the design load—and performed so well that it was obviously over-designed. (The Johnson Street socket length has already been reduced by 30 per cent on the basis of testing carried out so far.)

Unknown factors

According to Williams, present design methods do not take into account factors affecting the load-bearing capacity of the pile, such as strength of the rock, its compressibility, roughness of the socket, and socket length and diameter. Further research would separate out these factors and measure their relevance to design methods.

While Williams is making experimental field investigations into the performance of the piles, Sloan is engaged in theoretical research, examining the behaviour of the piles by means of finite element techniques.

The third step, which should synthesise the practical and theoretical work, is the intensive laboratory testing which has yet to be done. Johnston says, however, that the agreement between theoretical and experimental results has so far been most encouraging.

The problems associated with building on soft rock such as mudstone are not peculiar to Melbourne. They were not a great problem for the city until it began running out of space and building higher and heavier.

Wide application

Johnston says the reason why Melbourne is solving its own problems and not drawing on overseas experience is simply that most other cities sited on comparable geological formations are going through similar processes of experimentation.

He says he is confident that the Monash research will have useful application not only in other Australian cities, but also in other countries, most of which have soft bedrock.

In one animal killed 48 hours after treatment there were only a few tumor cells remaining in the sections examined and the tumor had become a shapeless mass containing granules which the researchers describe as "the garbage from broken down cells".

Dilated blood vessels and areas of haemorrhage were no longer apparent.

In tumor sections taken from other animals killed 48 hours after treatment, the changes were less marked.

Rapid action

The electron microscope revealed more details of the damage. It showed that only one hour after treatment there were obvious changes in the mitochondria of individual cancer cells and in the membranes connecting them.

Many mitochondria were swollen, showed a breakdown in their cristae (internal, bar-like ridges), and were filled with a cloudy material.

The cytoplasm surrounding the cancer cell nucleus was frequently filled with empty vacuoles (sack-shaped spaces) and other irregularities. And even the nuclei of some malignant cells appeared to be undergoing changes.

Similar internal changes in the malignant cells was evident in specimens taken two hours after 5,6-DHT treatment.

Starting point for the research was numerous studies which have shown that substances known as biogenic amines are an important factor in the rate at which both healthy and cancerous cells multiply.

Early last year, Tutton and Barkla found that inhibiting the natural production of a particular enzyme which breaks down biogenic amines would cause a spurt in the growth of colon cancer cells in their rats but not in the growth of cells in healthy surrounding tissue.

However, the enzyme only breaks down biogenic amines when they have been taken INTO cells, and not if they are acting only on a cell's OUTER MEMBRANE.

From these facts, Tutton and Barkla guessed that the amines act internally on colonic cancer cells but externally on cells of surrounding healthy tissue.

Through their research, they then discovered that the hormone 5-hydroxytryptamine is an important amine acting to stimulate cell growth in experimentally-induced cancers of this type.

Tutton then reasoned that if the cancer cells were absorbing this amine while healthy cells did not, then they might also absorb a toxic cousin such as 5,6-DHT, possibly with fatal results, while healthy cells remained unaffected.

The results of their experiment initially appear to support this guesswork.

MONASH REVIEW APRIL, 1977
Cheaper electricity?

MONASH chemical engineers have developed a process which they believe can slice millions of dollars annually off the cost of electricity generation in power stations burning brown coal.

It would reduce, by hundreds of thousands of tons a year—the coal that needs to be mined for this purpose.

As well as cutting the fuel bill of existing power stations, the system would also reduce, by about 16 per cent, the capital cost of building new ones.

And—perhaps more importantly—it provides a vital step for the conversion of brown coal to liquid fuel.

The process is the result of research by the chairman of the University's department of chemical engineering, Professor Owen Potter, and calculations by professional officer Mr Andrew Keogh.

It provides a simple, cheap way of drying off the moisture which makes up as much as two-thirds of brown coal.

At present, brown coal power stations are constructed with expensive, oversize boilers to enable this moisture to evaporate during the actual burning process.

Much of the heat energy produced is wasted in fueling this evaporation.

The Monash process, which can be added to existing stations, dries out 90 per cent of the moisture from the coal before it goes into the boiler—at a fraction of the energy cost.

Potter says it would result in an estimated minimum reduction of about 8-4 per cent in the amount of coal needed to produce the same amount of electricity. In a more expensive high pressure form, the dryer could increase this saving to about 13.8 per cent.

Details of the process are at present being withheld pending patent applications, he says.

As a basis for their cost-saving calculations, Potter and Keogh used the Yallourn W power station in Victoria—the state's largest with a capacity of 350 megawatts.

It burns 5.13 million tonnes of wet brown coal a year, but because of the fuel's moisture content, the boilers operate at only 65 per cent efficiency (based on the gross calorific value of the fuel).

This efficiency would increase to 82 per cent if the coal was first dried via their process, they calculate. Coal consumption would be reduced to 4.68 million tons a year—a saving of 460,000 tons.

Savings add up every second

On a 1971 financial basis, Yallourn W costs 29.5 cents per second to operate. In a new station of similar size incorporating the dryer system, this would be reduced to 25.3 cents.

"That 4.2 cents per second saving adds up over a year to $1.32 million," Potter points out.

Put another way, the cost of producing a kilowatt hour of electricity would be reduced from Yallourn W's present .378 cents to .324 cent.

And in addition, the new process offers additional benefits by reducing the capital costs involved in building a new power plant, the Monash engineers claim.

While the price of a 350 megawatt station (1971 costs) is around $60 million, this would be reduced to about $50 million if it was designed to burn brown coal dried by the new process, says Potter.

Most of this saving, which brings the price down near that of one burning high-quality black coal, would come from being able to use smaller boilers.

"Adding a dryer system to an existing station would cost about $2.2 million and because of this would not reduce unit costs. But it would at least pay for itself," says Potter.

"And it would immediately offer full savings on the amount of coal needed to maintain the same power output."

He would like to see Victoria's state power authority, the State Electricity Commission, add one as a pilot plant to one of its smaller stations. The cost, he says, could be partly met by the Victorian Brown Coal Committee, which has a vital interest in the future conversion of brown coal to liquid and gaseous fuel.

He feels that it is in this area that the dryer could have its greatest impact, as it produces a coal which is in ideal condition for conversion by twin processes known as pyrolysis and hydrogenation, or for solvent refining.

Pyrolysis, used to produce household gas is a high temperature treatment which releases fuel liquids and gases from coal. Hydrogenation involves adding hydrogen to the carbon-rich residue to produce a further yield.

In solvent refining, coal is dissolved under pressure in a heavy aromatic solvent derived from the process. The solution is filtered and fractionated to recover the solvent for re-use.

Twin projects seek way to defeat syphilis

A TWO-PRONGED research effort has been started at Monash aimed at developing a vaccine to give protection against syphilis, the most dangerous of the venereal diseases.

Medical investigators have been trying to produce such a vaccine ever since the organism which causes syphilis was first isolated in 1906.

The twin Monash projects aimed at its development are being run by a team headed by Dr. Stephen Graves, lecturer in the University's department of microbiology and including Dr. Timothy Billington and Mr. Ian McLean.

And he is confident that one or both will prove successful.

The first project is seeking a method of growing Treponema pallidium, the human syphilis organism, as a laboratory—"test tube"—culture. The failure of scientists to perfect a suitable culture medium in which it will grow has been a major stumbling block to the development of a vaccine.

Graves explains that human syphilis bacteria grow only in man and rabbits.

This means that laboratory samples at present can only be obtained by growing small quantities in inoculated rabbits.

"This presents two drawbacks," says Graves: "First, it has meant researchers have never had available the billions of bacteria needed for full-scale experimentation.

"Secondly, it is likely that any vaccine will be required to contain a large number of bacterial cells . . . either weakened or completely dead. And if these were grown in rabbits and not in laboratory culture medium, it would be almost impossible to rid the vaccine completely of rabbit protein. Such animal protein could cause an adverse reaction in people receiving it."

The second of the new Monash projects involves an attempt to develop a vaccine from an organism responsible for a different type of syphilis which infects only rabbits.

"So far as I'm aware nobody has ever . . . continued back page
'Flu test proves vaccine protection

IT PAYS to have a pre-winter influenza vaccination, according to a Monash study. In most cases, researchers have found, it does keep the "flu at bay.

They tested the effectiveness of the standard vaccine in a mass trial conducted during last winter’s epidemic caused by the A/Victoria flu strain. And it produced a protection rate of 80 to 90 per cent.

The research was a project of the University’s department of microbiology and used 229 volunteer "guinea pigs" from among staff and students of the Monash Medical School at Melbourne’s Alfred Hospital, including the department’s chairman, Professor Solly Faine.

The final findings were reached only after months of painstaking analysis of blood samples taken during the trial period and of a vast complexity of statistical possibilities.

CSL co-operation

The Monash project was carried out with the co-operation of the Commonwealth Serum Laboratories, who manufacture all influenza vaccine used in Australia.

Volunteers were randomly divided into six groups and vaccinated between April 2 and 5 last year. But only three groups, comprising 118 people, received influenza vaccine. The other groups, totalling 111 people, were inoculated with a placebo, or "fake" vaccine, of similar appearance. (It was, in fact, adult diphtheria-tetanus toxoid.)

The trial was conducted as a "double blind", in which neither volunteers nor researchers were aware who had received an influenza vaccination and who had been given the placebo.

To achieve this, a staff member not involved in data collection or interpretation secretly arranged the random groupings and vaccination schedules. His "code" was only broken when it came time to collate the final results.

Lecturer Dr. Leigh Hammond supervised the trial in collaboration with laboratory manager Mr. Tom McAvan and Dr. Allan Ferris, a reader in the department.

Ferris, one of Australia’s leading virologists, is also one of three permanent members of what is known as the Influenza Vaccine Committee. The committee meets annually to decide the composition of Australian "flu vaccine to be produced by the Commonwealth Serum Laboratories for the coming winter.

Despite this involvement with the supply of vaccine, Ferris says that until the Monash trial he was sceptical about its effectiveness. "In fact, most members of this department were of the opinion that there was no conclusive evidence in its favor," he says.

Firm evidence

He believes the trial has provided evidence that standard "flu vaccines given at optimal times can be effective.

It is significant, he points out, that a comparable percentage of volunteers in both the vaccinated and placebo groups came down with "non-flu" respiratory illnesses.

Of the 118 people vaccinated with influenza vaccine, 62 (53 per cent) reported infections which were diagnosed in the "common cold" or "upper respiratory tract infection (URT1)" categories.

Among the 111 who received the placebo, 55 (50 per cent) suffered similar illnesses.

"In other words, the results indicate that the volunteers had an equal share of winter coughs and colds, but when it came to influenza the group who received the genuine vaccine were protected," Ferris explains.

The incidence of laboratory-confirmed "flu cases among the Monash volunteers coincided with the rise and fall of the "A/Victoria" epidemic among the general public, when compared with statistics compiled by the Virus Diagnostic Laboratory at Melbourne’s Fairfield Hospital. (See graph.)

The epidemic peak was recorded in the last week of May and the first week of June.

"From this comparison, we know that the effectiveness of the vaccine was tested under optimum conditions," says Ferris.

Hammond points out that the protection... continued back page
The 'good oil' on waste oil

RE-REFINING the used oil drained from Australian cars is not economically worthwhile, according to the results of a Monash-based study.

For the present, blending of small amounts into fuel oil appears to be the only economic recycling option available, say engineers involved in the research. This would still make a valuable contribution to the country's resources conservation effort, they point out. Every barrel of used lubricating oil burned as fuel in, say, furnaces means one less barrel which has to be imported.

Chemical engineers involved in the study examined 10 new and traditional re-refining techniques but decided that none was suitable for use in small-scale Australian-style plants.

In 1970 there were seven of these in operation but all but one are now out of the re-refining business. Examining the economics of the industry, the researchers concluded it was basically as cheap to make fresh lube oil, despite the present high price for Middle East crude.

The study was made by engineering science masters student Don Siemon, supervised by Associate Professor John Agnew. The work was funded through a scholarship awarded by Mobil Oil Australia Ltd.

A report on their findings will be presented as a paper to "CHEMeca '77", the fifth Australian conference on chemical engineering, to be held in Sydney in September.

Agnew says the death-knell of Australia's re-refining plants was sounded by a combination of two main factors:

- The evolution of oils containing a variety of additives to improve lubricating performance but which make re-refining more technologically complex.
- The policing of stiffer environment protection legislation, which frowns on such re-refining plant effluents as waste acids, oily clay sludges, and objectionable odors.

"What's needed to change the situation is a much better processing technique and what that involves is much more expensive technology. What we've done on costing in the current study is based on the absolutely basic, old-fashioned acid-clay process," says Agnew.

"And that, in any case, is nowadays not giving a re-refined product which is good enough.

"Any technique that is more sophisticated will cost more money if it is tried on the same scale we've seen in Australia up to now. The only way you could bring that cost down is to increase the rate of treatment...you've got to collect more waste oil and you've got to process more."

Because it is basically as cheap to produce fresh lube oil, there is at present no financial incentive for oil companies to purchase and remarket re-refined oil from small processors, the Monash study points out.

As well, lube oil refineries are working below capacity. They are capable of producing 600,000 cubic metres of fresh oil a year but demand at present is only 500,000 cubic metres.

The annual consumption of automotive lubricating oils in Australia in 1975 was about 270,000 cubic metres. It has been estimated that two-thirds of this is eventually drained from sumps and gearboxes, creating a huge disposal problem.

While oil companies use some (about 25 per cent) for blending in fuel oil and some, in the past, has been re-refined by the now defunct private operators, much of it is dumped.

The Monash engineers warn that these dumped wastes can constitute a serious environmental hazard—one recognised by legislation in the U.S. but not here.

Future increases in imported crude oil prices could swing the economic balance back in favor of re-refining used oil, even with existing technology, the researchers say.

The situation could also change should the government clamp controls on disposal methods or introduce a West German scheme whereby a "deposit tax" is added to each can of oil similar to the deposits on some soft drink bottles.

In West Germany, this encourages waste oil collection by individuals and small businesses and its delivery to central depots for re-refining.

However, the report adds, the tighter environmental controls now being imposed may even then prove too expensive for the relatively small re-refiner to meet.

Syphilis project

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tried this approach with any degree of determination," Graves says.

His hopes in this direction rest on comparable earlier successes in the field of immunology, such as the use of a virus derived from cow pox to give protection against smallpox.

Graves, a Monash Ph.D. graduate who recently returned after two years at the University of Minnesota, has so far received financial backing for the new project from the National Health and Medical Research Council, the Ian Potter Foundation, and from the estate of the late George Adams, founder of Victoria's Tattersall's lottery.

But like many other researchers, he anticipates a significant portion of his energies will be needed for fund-raising to keep the work going.

Graves is convinced that the development of a syphilis vaccine is a matter of urgency.

"The incidence of the disease is increasing at an alarming rate," he says. "It is currently ranked third among notifiable diseases in Australia, exceeded only by gonorrhea and infectious hepatitis.

"From 1966 to 1975, the number of notified cases rose from 6-8 to 17-6 per 100,000 head of Australian population. The rate of increase was 138 per cent between 1966 and 1974. Between 1973 and 1974 alone, the increase was 50 per cent.

"The current incidence of syphilis in Australia is higher than in the United States."

'Flu vaccine test

from previous page

tion rate in the groups who received the influenza vaccine is made more impressive by the fact that all volunteers were working and studying in a relatively confined area.

"Each would be likely to have more contacts with influenza than a person in the outside community," she says. "This would particularly apply to staff members of the microbiology department who took part. Here influenza cases among the placebo group were in close contact with the vaccinated group and challenged their immunity."

The researchers say another finding was that six volunteers in the placebo group and seven of those who received "flu vaccine had some antibodies against "A/Victoria" influenza before they were inoculated.

The antibodies were detected in blood samples taken at the start of the trial.

"Their presence supports the common theory that new strains of influenza virus may be around for 12 months or more before appearing in epidemic proportions," says Ferris.