12

5th Kumaradasa Rajasuriya Memorial Oration

Malaria

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We are gathered together today to remember and to honour the late Professor Kumaradasa Rajasuriya, Professor of Medicine in the University of Colombo.

Professor Rajasuriya had a strong influence on my professional life and I am therefore greatly honoured to have been invited to give this oration. I would like to thank the Professor Kumaradasa Rajasuriya commemoration committee for selecting me.

As a physician, Professor Rajasuriya was exceptional in the universal care and concern he extended to all his patients, rich and poor alike. The way his patients faces lit up when his neat and dapper person entered the professorial ward was testimony to their faith in him as a caring and brilliant physician.

As a teacher, his meticulous concern in teaching us to elicit physical signs was invaluable in those early days of medicine when echo-cardiograms, ultrasonograms, CT and MRI scans were unheard of. He always corrected us with a firm but kindly smile and made sure that we understood.

As an examiner he was always scrupulously fair, never rattling nor upsetting an examinee.

As a Research scientist his keen and sharp intellect kept any paper clear and concise. He even found time to correct and to put into perspective one of my earliest efforts, on this very subject of Malaria.

It is little known that Professor Rajasuriya very nearly specialised in Paediatrics, having been a registrar at the Ridgeway and having worked at Great Ormond Street and passing his DCH.

It is a measure of Professor Rajasuriya's concern for his country that when the second great malaria epidemic of the late 1960s was starting, he brought a team to Anuradhapura to see for himself. I remember him and his team catching mosquitoes and larvae from very remote villages. Professor Rajasuriya found time to talk kindly to these deprived people and told us of the very serious consequences that would follow if Malaria were to come back.

At the end of a hard day he sat with us at the ruined monastery at Tantrimale, one of our lesser known of our places of worship. Here the Professor showed us other sides of his nature, his intense devotion to his religion, his love for his country and his wide knowledge of its history.

For Professor Rajasuriya, every aspect of the practice of medicine brought him joy. He was the very epitome of a person who practised both the science and the art of medicine to perfection. His interests went beyond the hospital to the welfare of the community and the country. This led him for a while to take on the onerous task of Director General of Health. He was truly a man worthy of emulation. For a start do read carefully his parody of Kiplings famous poem, 'If' (see page 56 in this journal).

Malaria is not just a 'febrile illness' but a preventable disease which has major effects on the health and the productivity of our farming communities with effects on regional economies.

As we all know, the word 'Malaria' is from Latin and means, 'bad air'. Which was thought to cause the disease. This is the oldest disease to have affected mankind. David Suzuki the Canadian

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naturalist believes that half the people who ever lived on earth had it at some time in their lives.

The mummies of ancient Egyptian rulers showed enlarged spleens and livers which are thought to have been caused by Malaria. The ancient Chinese called it 'The Mother of Fevers'.

Hippocrates was one who associated fever with marshes and which he called the 'Marsh Ague'. His description of the disease which affected those who he thought drank the stagnant water was, "of having large stiff spleens and hard thin hot stomachs while their shoulders, collar bones and faces are emaciated;" He said "the fact is that their flesh dissolves to feed their spleens."

McNeill in his book, 'Plagues and Peoples' describes how parts of Italy which were dense farming communities in the 5th to the 3rd centuries BC became Malarial wastelands. Explorers found the river basins of Africa and of the new world to be hotbeds of fever.

An important finding from Peru in the 1650's was that the natives who got fever, used an infusion of the bark of a tree to relieve their symptoms. This was brought to Europe, named after a Spanish countess and thus cinchona became known to the world of medicine. Quinine was extracted from it some 200 years later. When the coffee blight destroyed crops, attempts were made to grow the plant in this country.

Today, WHO statistics show that 2.5 to 3 million die from malaria every year. Morbidity figures may be impossible to count but are assessed as being between 300 and 500 million a year. The disease is distributed throughout the tropics and some temperate zones being specific to river basins in heavily forested areas and to marshy land. Levers in his 'Manual of the NCP' gives us the best description of the common, chronic form of the disease as he saw it in his area He said "One is never really ill nor is one ever really well".

It is interesting to note that none of the chronicles of Sinhala, The Mahavamsa, the Culavamsa nor the Dipavamsa made mention of a fever which could have been Malaria, while mentioning famine, and illnesses which could have been cholera yaws and even leptospirosis.

An ancient treatise of Ayurveda dating to the medieval period translated by A Cassey Wood and reprinted in 1926 describes 'Kanjika' a sour liquid made from fermented powdered paddy. This yielded a clear transparent fluid. with an acid taste and a vinous odour which was given as a cooling drink to thirsty patients living (and dying) of fevers. Dr John Attygalle describes it as also being used as a cold compress.

'Kela Una' is the term used to describe fevers with ague by the traditional physicians of the Rajarata.

In the ancient ritual of the ***'Daha ata Sanniya'***, the eighteen demons that mimic common symptoms, ***'Vevulum Sanniya'*** (shivering) ***'Seethala Sanniya'*** (Cold) and ***'Maha Ginijal Sanniya'*** (High Fever) could be related to Malaria.

The American geographer Rhoads Murphey writing to the Journal of the Royal Asiatic Society in 1957 claimed that the collapse of the Rajarata civilisation was due to Malaria. The disease, he says, was brought to the area by infected troops of the invading Cholan armies. It is claimed that Magha, the Cholan invader in 1215 AD captured Polonnaruwa by breaching the bund of the Parakrama Samudra. Murphey further stated that, once debilated by Malaria the resident population was unable to maintain the elaborate social and administrative structures of rajakariya to repair and maintain the tank irrigation systems.

Drought, illness and famine was registered in the reign of Parakrama Bahu II in the 13th century, and the capital shifted, southwestwards and finally to the central province.

In his work, Murphey also ruled out climatic changes as a cause of this migration. Dennis Fernando differs: in a study of aerial photographs of the area particularly around the Somawathiya Chaitya. He claims that the Mahaweli ganga had changed its course during this period. Thus leading to disruption of the irrigation of the entire area and leading to a climatic change.

Early foreign travellers, Pliny (45AD) Fa Hsien (414 AD) and even as late as Ibn Batuta (1344 AD) spoke of our country in glowing terms and none made any mention of a serious fever.

It may seem therefore that malaria was unknown in the golden years of the Rajarata and only appeared around the thirteenth century finally leading to abandonment of the area from mass migration.

While there has been little mention of this disease in the early chronicles of the nation, the various invaders to our shores made much of it. The Portuguese, Barros and Couto in 1573 were more concerned about commerce but did make sad mention of the fact that Pero Vas, Viceroy designate from Goa died of 'certain fevers' within seven days.

Father Fernao de Queyroz in 1687 wrote that the ancient court of Anuradapura was abandoned due to the prestilence of recurrent fever which attacks the same person 2 - 3 times. He also speaks of a quartan fever or ague, like a general pestilence which has buried many. Ribiero writing about the diseases affecting Portuguese settlers, mentions dysentery and some kinds of fever "due to the poverty of blood."

In 1672 Phillipus Baldeus, a minister of the Word of God, writes of the last day of the 'Empress Dona Catharina who was with child and fell dangerously ill with a fever. She is said to have lost her senses but subsequently recovered and then died. Wickramasuriya in 1936 writing on Malaria in pregnancy, observed that in cerebral malaria, this lucid interval, which he called 'the called 'the calm before the storm' carried a very serious prognosis.

During their occupations, both the Portuguese and the Dutch, were more interested in their revenues and had little thought for the people of the country. Francois Valentijn said that, "among them, the pox and the fever strongly, from which each must protect and heal himself of these.; there are no doctors or surgeons here."

Of the British, the most famous was Robert Knox who was for many years a captive of the kings of Kandy. In his 'Historical Relation of Ceylon' published in 1672 he refers to the interior of the country being "suddenly desolated by endemic fever." He continues that "When first we used those parts, we used often to be sick of violent fevers and agues when we came home. People that dwelt upon the mountains as we did, whensoever they went down into these places and commonly the major part of them that fall sick, dies". At length they found an antidote and counter poison that" after the use thereof we had no more sickness." The cure "was only a dry leaf; "they call it the Portuguese Banga, beaten to a powder with some of the country jaggery. This we eat morning and evening on an empty stomach. It intoxicates the brain and makes one giddy without any other operation either by stool over vomit".

Dr John Attygalle in his Material Medica states that the Sanskrit word 'Banga' is what we call "khansa or ganja' and which the world calls 'Cannabis' or Marijuana' and which was a favourite medication among Ayurvedic practitioners as a febrifuge. Did Knox, in fact, survive because of some anti malarial action of this drug?

Marijuana is being tested for its medical effects in reducing pain and muscle spasm, has it in addition an action against the malaria parasite?

Chaplain to the Garrison of Colombo in 1800, The Revd James Cordiner while commenting that Trincomalee was "the least healthful of the stations we now occupy in Ceylon" also made the interesting observation that "the fever that raged at these periods was not contagious".

In his book, 'The Great Rebellion of 1818', Professor Tennakoon Wimalananda said that "the Southwest monsoon came unusually late in 1818 and added very heavily to the list of the sick and prevented execution of Brownrigg's plan of suppression. The British Army were baffled by the types of fever and dysentery". Malaria caused great problems for invading armies perhaps far more than to the native inhabitants and could probably be thought of as a actor in our favour.

Paul E. Pieris in his book 'Sinhala and the Patriots' speaks of army hospitals which were sheds thatched with coconut branches. Cerebral Malaria was playing havoc and most of the victims died raving mad. But the type of fever varied with the locality in a manner which was inexplicable.

John Davy, MD FRS in 1821 said that intermittent and remittant fever are justly considered as varieties only of the same disease. He added that there was a strong tendency to delirium.

Sir James Emerson Tennant in 1859 wrote that "half way between Colombo and Kandy is the picturesque rest house of Ambepussa, one of those treacherously beautiful spots which have acquired renown from the attractions of its scenery and the pestilent fevers by which the locality is infested."

After millenia of causing misery and death to the human race, the parasite was finally isolated by Alphonse de Laveran in 1880. In 1898 a Scottish doctor in the British Army in India provided the proof of the mode of transmission. Sir Ronald Ross in his moment of triumph was able to claim, "I have found thy secret deeds, O murderer of millions."

Hirsch in 1893 was the first to use the word Malaria when he referred to our country as "one of the headquarters of a severe, remittant and pernicious Malarial fever."

The most sympathetic of the agents of the colonial government, Leonard Wolff, in his diaries in 1908 speaks of the Hambantota Hospital "where accomodation was quite inadequate; most of the cases are Malaria". He goes on to say "the pearl divers never get fever which confirms my belief that sea bathing helps to keep off Malaria." And later "In Magamputtu these villages are decimated. It is an awful sight to see the children".

Dr H.F. Carter in 1927 wrote that "the fever season is from the beginning of November to the end of February in many parts of the dry zone." He wrote that the 'Spleen Rate" in children afforded the most accurate guide to endemicity. A rate of 10% to 40% indicated a low endemicity whereas rates of 40% to 60% indicated high or very high endemicity. Medical entomologist Carter said that of the mosquito species, only Anopheles culicifacies needed to be considered.

Col C. A. Gill LMS, MRCP(Lond), DPH, DTM&H who was Malarial Officer of Ceylon, Burma and the Punjab put forward a scheme for Malaria control but this was disregarded. He stated that the Deduru Oya and the Maha Oya and to a lesser extent the Kelani and Mahaweli rivers were mainly involved.

Our own researches at the Public Records Office (National Archives) in London revealed that an 'Anti Mosquito Ordinance' was narrowly outvoted in 1933 in the State council in spite of the vigorous efforts of George E de Silva.

The stage was then set for the great Malaria Epidemic of 1935/36 where with partial failure of both monsoons, over 80,000 deaths 30,000 of them children occurred over a short season mainly in the basin of the Maha Oya 'The Malaria River' involving Kegalle and Kurunegala also of the Deduru Oya. Morbidity could not be recorded but was assessed at around 1/5 the population of the country. The extent of the death and devastation caused by this epidemic was quite unforessen. All the resources of the department of Medical and Sanitary Services were mobilised as well as the services of many private practitioners.

Col Gill sadly recorded that this was the worst pestilence in the recorded history of the country. The DMSS Dr Briercliffe and Dr Dunn painstakingly recorded this epidemic in their monographs.

Belatedly the State Council allocated 114,000 dollars for relief work and called for public donations. This was many times that which would have been needed for the anti mosquito ordinance. His excellency governor Newnham however assured the public that the weekly relief payments would reach the hands of the affected peasants. An attitude which is worthy of emulation by aid giving agencies throughout the world even today.

The then new drug Atebrine Mussonate was used in certain large hospitals as well as in the field for remote villages. The results were reported as being good.

Malaria played a very important role in World War 2 in the East. The British Army, conscious of the losses of its forebears in the country took extreme measures to keep this disease in check.

Malaria discipline was very strictly enforced. Between dusk and dawn the use of shorts and short sleeved shirts was banned. All ranks had to sleep under mosquito nets and if leaving to go out even to the toilet, had to cover their exposed areas with a repellant ointment. Mosquito breeding areas were drained or sprayed with oil and pyrethrum sprays were used both within the camp and outside it.

An interesting feature was the daily 'Mepacrine parade' where all troops were paraded and an officer walked down the ranks putting a tablet into the mouth of every soldier. An orderly followed with a drink of water after which the soldier had to call out his name loudly as proof that he was not keeping the tablet in his mouth. In spite of these draconian measures which were rigidly enforced the strike rate was 2½ attacks per man per year.

A file of malaria as it affected the South East Asia command (SEAC) records a meeting with a doctor from the Pacific command which included New Guinea and the South Pacific islands. He claimed that in his area the Malaria rate was only one eighth that of SEAC.

Lord Louis Mountbatten, the Supreme Allied Commander is said to have 'blown his top' and demanded immediate action. This is how DDT spraying came to Ceylon. It is likely that DDT emulsion was also sprayed from the air using B25 bombers fitted with 500 gallon tanks instead of, bombs particularly. In the Hingurakgoda and Pelvehara area where the American B29 Superfortress bombers were to be based.

A subfile of this was titled 'Malaria as a Weapon". Although it had been declassifed after 50 years the file was empty. It would have been interesting to see if Lord Mountbatten planned to carry out this very early attempt at microbial warfare. Malaria did have its effect and is was thought that the attempted Japanese invasion of India through the Arakan failed because the Japanese army was decimated by Malaria.

By the end of the war, Malaria was controlled to the extent that Prime Minister D.S.Senanayake could go ahead with plans to repair the great tanks and irrigation schemes and bring in the landless to colonise these hitherto uninhabitable lands. Relentless work by the antimalaria campaign brought morbidity down from 2 million in 1946 to 17 reported cases in 1963. When we were students in the late 1950s Professor Rajasuriya spoke often of Malaria but had no cases to show us!

Insecticide spraying was finally stopped on the advice of W.H.O in 1964. In 1963 the annual parasite rate had fallen to less than 0.005 per thousand.

Illicit gem miners in the Laggala-Pallegama area left open gem pits which filled up with stagnant water and bred anopheles. There were pockets of the parasite in the very remote villages and the two came together to infect the invading gemmers who then fled to their home villages carrying the parasite to areas where the vector was now breeding actively. Two further accidents contributed to the confusion. Microscopists, who worked in a building opposite our house, examining blood films had some disagreement with the AMC and were on a go-slow creating a backlog of slides of some three months.

These out of date statistics blinded the Department of Health Services to the true situation. There was Malaria everywhere but no response save for a circular ordering the transfer of all fever cases to provincial hospitals. The major pilgrim destinations of Anuradhapura and Kataragama further helped to spread the parasite.

A rise in morbidity from 17 in 1963 to 440,644 in 1968 heralded the tragedy of the Second Coming of Malaria.

The leading players in this tragedy of Malaria are the plasmodia, falciparum and vivax.

Malaria in its classical form is intermittent or remittant fever with chills and rigors. Deaths are now uncommon in this country unless the severe cerebral form occurs.

The late Professor P. B. Fernando taught us that Malaria was the great imitator of disease. No medical presentation on fever would be accepted unless Malaria was mentioned in the differential diagnosis.

Almost every system in the body can be affected by Malaria.

Neurological

Cerebral Malaria
Febrile fits. This especially in children under 5 and due to the sudden rise in temperature.
Toxic confusional states
Guillain Barre like Syndrome
Extrapyramidal tremor
Delayed Psychosis
Acute Cerebellar Syndrome. Dr Anula Wijesundera reporting from Polonnaruwa found this in 23.8% of her series.

Gastrointestinal

Persistent Vomiting and Diarrhoea with Choleraic and Dysenteric form common in Children.
Hepatitis and even **Hepatic Encephalopathy.**
Biliary Remittant Fever.
Herpes Labialis
Splenomegaly.

Haematological

Anaemia with rapid fall of Haemoglobin to <7.8G/dl (50%) Classical. Microcytic, Hypochromic with increase in mononuclears.

Cardiovascular

Anoxic Hyperventilation from very severe anaemia resulting in death unless relieved urgently by very slow packed cell transfusion.
This was most often seen in acute intravascular haemolysis from G6PD deficiency.
Congestive Cardiac Failure from chronic persistent anaemia was a more common finding.
Peripheral Circulatory Failure. Algid Malaria. This is a rare but serious manifestation. There is severe shock requiring inotropic sympathomimetics and plasma infusion. Few have survived.

Renal

Acute Nephritic syndrome particularly with falciparum infections. With oedema, oliguria, haematuria and hypertension.
Nephrotic syndrome was reported by Wijesundera.

Pulmonary

Cough with bronchitic picture especially in children
Acute Pulmonary Oedema requiring intravenous frusemide.

Systemic

Tropical Splenomegaly Syndrome, with hepatosplenomegaly, anaemia, leucopaenia and thrombocytopaenia. Malarial antibodies are high and a liver biopsy will show malarial infestation.

Nutrition

Malaria and Nutrition. The effect of Malaria on rural populations already suffering from undernutrition, anaemia and vitamin deficiency is hard to assess. Many babies are handicapped by being small for dates. Growth faltering is likely to occur in children upto 5 years and

adults to suffer from anaemia, lethargy and poor work output.

Hypoglycaemia occurs with severe falciparum infections and may result in convulsions.

Pregnancy

Malaria and Pregnancy In 1936, Professor G. A. Wickramasuriya working at the height of the epidemic carried out meticulous dissections of the placentae and postmortems on stillborns and neonatal deaths. He demonstrated parasites in the placentae, cord blood and brain, spleen and livers of the dead infants and suggested that with heavy falciparum infestation and inadequate treatment of the infection, damage to the placenta could lead to Malaria infection of the foetus.

He insisted that intravenous quinine was not oxytocic but that the disease was, leading to abortion and stillbirths and premature delivery. He said that the drug must be used vigourously to save mother and baby especially in cerebral malaria. Working with only a microscope and a haemoglobin scale he was the first Sri Lankan to win an international prize for Medicine for his demonstration of transplacental foetal infection with malaria.

Post Malaria Syndrome

This is probably commoner than suspected. Anula Wijesundera in her series showed that nearly 6% complained of ar thralgia, anorexia loss of energy and head ache. It is easy to understand the effect that this can have on the work output of an agricultural economy.

Recurrent Malaria

This is a feature of the disaese and is responsible for much of the debilitating effects seen. This could be a relapse or a reinfection. Vivax treated with quinine only been known to relapse many years later and pursue its foreign victims back to their homes.

In the absence of a vaccine, chloroquine prophylaxis may be indicated. This is difficult to maintain and carries the risk of chloroquine amblyopia. A major cause of relapse is lack of patient compliance. Here, drugs are stopped as soon as the fever subsides without completing the course.

This is a problem that offers scope for intensive patient education. In the 1980s the then Director General of Health, Dr Malinga Fernando arranged a programme of AMC officers and some physicians to visit and talkto affected people at Gramodayamandala level in order to improve drug discipline and domestic measures of mosquito control.

In Sri Lanka the commonly used drugs are Chloroquine and Primaquine administered for 5 days as radical therapy. Drug resistance of certain Falciparum strains to Chloroquine has been noted. This is in the more serious Pii and Piii types

Primaquine sensitivity

This important side effect was first reported in this country in 1968 by Dr Kamalika Abeyaratne and Dr Neil Halpe from the Paediatric unit at Anuradhapura. An avalanche of children with acute intravascular haemolysis coincident with the Malaria epidemic heralded the use of Primaquine (Please see table 1)

At this point I must mention the late Dr Gladys Jayawardene then DDLS who was so prompt and helpful in importing the brilliant cresyl blue reagent essential for prov-

ing the cause of the intravascular haemolysis.

Glucose 6 phosphate dehydrogenase (G6PD) is a red cell enzyme. WHO estimates that over 41/2 million people world wide are deficient in this enzyme as a genetic defect.

This was disease described by Pythagoras as 'favism' 2500 years ago. The dramatic symptoms then were caused by eating the fava bean which is a staple food in parts of Egypt and the middle east. This contains pyrimidine derivatives Divicine and Uramil which are responsible for the haemolysis in G6PD deficient individuals.

Table 1

Summary of the first 21 children with acute intravascular haemolysis

No	Age	Sex	PRIMAQUINE		URINE			BLOOD			
			Dosage	Time of onset	Haemo-globin	Urobilin	Haemo-globin	Reticulo-cytes	Bilirubin mg/100 ml	Urea	G6PD
*1	3	F	1/2x5	5d	+	-	-	-	-	-	-
2	5	M	1/2x5	5d	+	-	-	-	-	98	GD
3	5	M	1/2x5	5d	+	n.l	12.1	-	1.7	32	PD
4	8	F	1x3	2d	+	+	-	2	0.9	32	GD
5	12	M	1x5	5d	+	nl		2	0.9	32	GD
6	8	M	1x2	1d	+	nl	9.4	4	4.5	47	GD
7	5	M	1x4	4d	+	nl	9.4	-	0.9	45	GD
8	8	M	NK	2d	+	+	-		1.7	80	-
*9	12-Sep	M	1/2x2	4d	+	-	-	-	-	-	-
10	11	M	1x8	5d	+	+	5.2	6.6	5.5	80	GD
11	51/2	M	1/4x1	1/2 d	+	+	6	1	3.7	60	GD
12	2	M	1/2x4	4d	+	-	-	-	3	-	PD
13	2	M	1/4x5	5d	+	+	-	25	4.4	60	GD
14	5	M	1x2	1d	+	+	4.8	-	-	84	NL
15	2	F	1/4x2	2d	+	++	8	1	2	42	GD
16	8	F	NK	2d	+	+	-	2	-	-	GD
17	11	M	1/2x3	3d	+	+	2.4	2	-	-	PD
*18	12	M	2x1	1d	+	+	7.2	2	-	375	GD
19	8	M	1/2x3	3d	+	-	-	2.5	5.8	30	GD
20	9	M	NK	3d	+	++	9.6	1	-	110	GD
*21	2	M	NK	id	+	+	-	-	-	-	PD

Dosages of Primaquine are expressed as fractions of a tablet of 7.5 mg

* Death - test not done NK not known

\+ test positive nl within normal limits

GD Gross deficient P.D. Partially Deficient

Drug induced haemolysis was first reported from Boston and from India after use of the antimalarial, Plasmoquin. Table 2 shows other drugs causing haemolysis is susceptible individuals.

Table 2

Drugs known to cause haemolyis in B negative form of G6PD deficiency

Antimalarials	**Antipyretic Analgesics**
Primaquine	Acetyl salicylic acid
	Phenacetin
Sulphonamides	
Cotrimoxazole	**4 Quinolines**
Sulphadiazine	Nalidixic Acid
Sulphadimidine	Ciprofloxacin
Sulphasalazine	
	Other antibacterials
Cardiovascular drugs	Chloramphenicol
Trinitrotoluene	Dapsone
Procainamide	
Quinidine	
	Miscellaneous
Other drugs	Methylene blue
Dimercaprol	Naphthalene
Menadione	
Probenecid	**Plant substances**
	Fava Bean
	Adathoda
	Acalypha Indica (*Kuppameniya*)

Infections are also known to cause Acute Intravascular Haemolysis

Table 3 shows, in the metabolism of the red blood cell, the enzymes of the pentose phosphate pathway. Of these, glucose 6 phosphate dehydrogenase, 6 phospho gluconate dehydrogenase and glutathione reductase are all susceptible to enzymopathic disease.

In human metabolism the Emberden Myerhof cycle accounts for 90% of glycolysis and the pentose phosphate pathway for 10%. Glucose 6 phosphate catalyses the first step in this pentose phosphate pathway, which is the only pathway in the human red cell. Therefore enzyme deficiency will leave the red cell incapable of producing Nicotinamide. Adenine di Nucleotide Phosphate NADPH in its reduced form. This in turn is required to maintain Glutathione GSH in its reduced form which in turn protects haemoglobin against oxidative denaturation.

To summarise, the red cells of G6PD deficient individuals are unusually sensitive to oxidative stress and when exposed, their haemoglobin undergoes oxidative denaturation to methhaemoglobin, which clumps away from the cell wall giving the characteristic blister cell appearance before undergoing haemolysis.

There are 2 main types of the G6PD enzyme. B+ and A+. The B variant is the common Mediterranean, middle eastern, asian and oriental form.

The A variant is that seen in Africa, and its deficient A- a mild form. The B- however is unstable giving severe form of IVH. This is what we have so far isolated in Sri Lanka.

The deficient trait is an X linked recessive; male neccesarily being hemizygous are more severely affected.

Malaria and natural selection

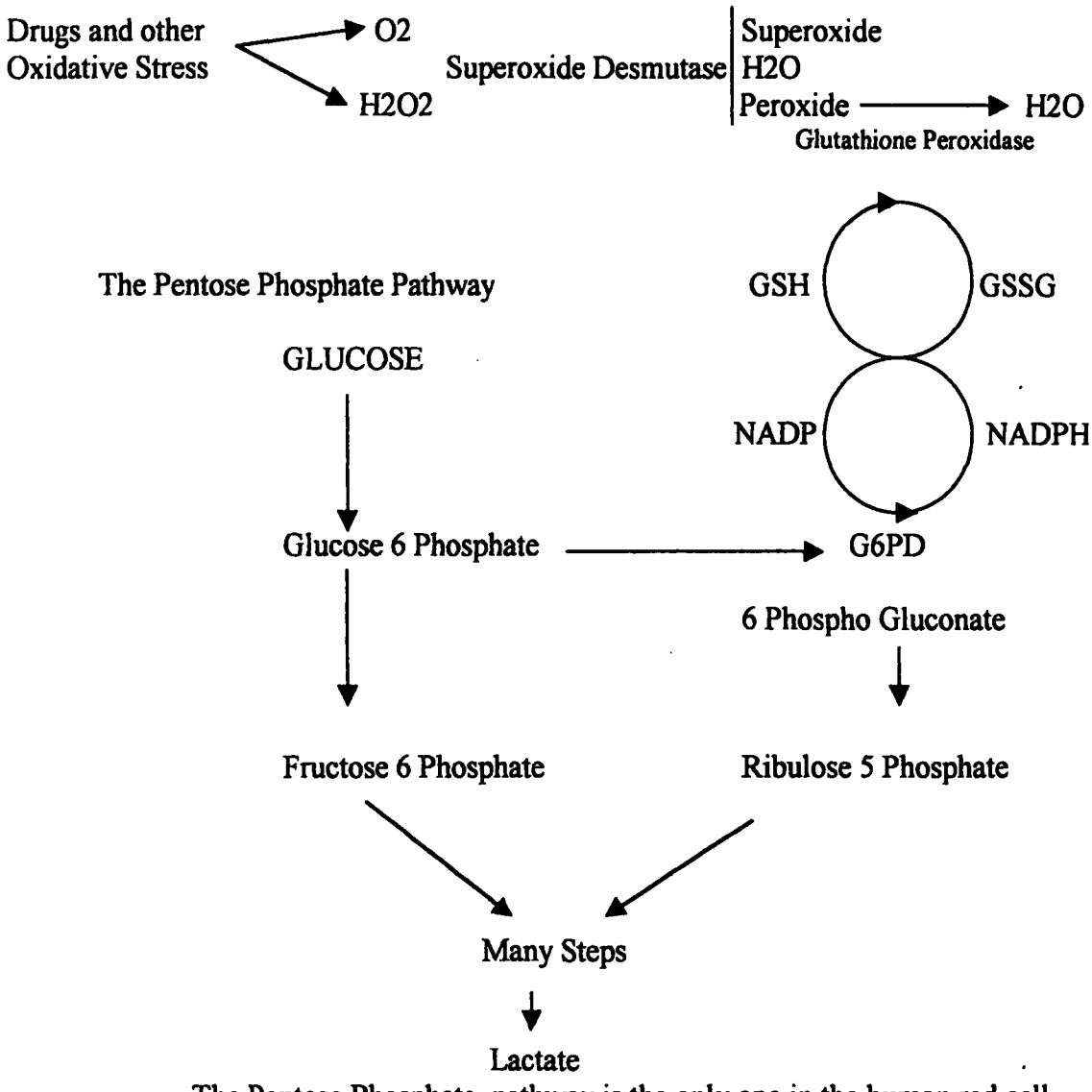
It is unusual to think of a disease like Malaria being responsible for natural selection but it does happen that P. falciparum finds survival difficult in enzyme deficient cells. This means that G6PD deficient individuals tend to be spared by falciparum malaria and that there would be a high proportion of deficients in falciparum endemic areas. The frequency of the gene in the population will also be increased by intermarriage as is seen in the 'Purana Villages' of the dry zone. The identical mechanism works with the selection of thalassaemia.

The incidence of neonatal jaundice is high in the areas of high enzyme deficiency.

Of the first 92 cases that presented to our unit after the use of Primaquine commenced in 1968, 60 were seriously ill and 10 died. This led to reluctance on the part of all staff both in the hospital and the field to prescribe Primaquine.

Table 3

Protective mechanisms against oxidative stress of the erythrocyte



The Pentose Phosphate pathway is the only one in the human red cell.

Table 4

Presentation of the first 92 cases

			%
A	Haemoglobinuria	92	100
B	Anaemia and Cardiac Failure	37	40.2
C	Anaemia and Renal Failure *4 required dialysis*	13	14
D	Anaemia with Collapse	6	6.5
E	Anaemia	36	39
Seriously ill B C D		56	60.7
Deaths		9	10

Table 5

Drugs involved as the cause of haemolysis

		%
Number of Children	92	
Primaquine	72	78
Aspirin	8	8.6
Sulphonamides	3	3.2
Traditional remedies	4	4.4
Infective Hepatitis	3	3.2
Typhoid fever	2	1.2

Table 6

The management of acute intravascular haemolysis

- Early diagnosis, immediate stoppage of causal agent.
- Therapy for shock and cardiac failure
- Blood transfusion, may be urgent
- Maintain hydration and good urine flow.
- Monitor urea, creatinine and serum electrolytes
- Management of renal failure

  Peritoneal dialysis is very effective and should be started early

  Diuretics and osmotic agents not found to be helpful

Further investigation was necessary and was carried out in collaboration with Dr D. F. Roberts of the Department of Human Genetics of the University of Newcastle upon Tyne and financed by a grant from the National Science Council.

Group A was our original 92 children (Table 4) whose deficiency was detected by the Brilliant Cresyl Blue test. All blood samples were sent to Newcastle upon Tyne for confirmation.

Group B comprised 272 blood samples from unrelated male patients from the Anuradhapura, Kalutara and Hambantota hospitals. All these sample were examined by starch gel electrophoresis at Newcastle and confirmed B- as our variant of the disease.

Table 7

Hospital samples from unrelated patients in surgical wards

Hospital	Number tested	Number deficient	Rate
Anuradhapura	132	7	5.3
Kalutara	100	5	5
Hambantota	40	1	2.5

Group C 1317 field screening tests were carried out in the same three districts using the fingerprick micromethaemoglobin reduction test of Knutsen and Brewer on unrelated males aged 8 to 14.

Table 8

District	Sinhala			Ceylon Moor			Tamil		
	Tested	Deficient	Rate	Tested	Deficient	Rate	Tested	Deficient	Rate
A'Pura	627	53	8.4	120	6	5	160	0	0
K'tara	100	2	2	100	1	1			
H'tota	104	2	1.8	103	2				

Table 9
Analysis of results by subpopulation

Area	Number Tested	Deficient	Rate
Vijepura *Suburb*	115	4	3.5
Kandalama *Colony*	104	7	3.7
Anuradhapura *Hospital*	132	7	5.3
Anuradhapura *School*	153	8	5.2
Hirigollegama *Purana Village*	113	8	7.1
Vihara Bulankulama *Very remote purana village*	139	29	20.9

Here I must pay tribute to my registrars, Drs Premawansa, Lalani Rajapakse and Padma Ariyawansa and thank them for their efforts without which this work would not have been possible. At one remote site we could not complete reading the tests as there were elephants on the track so were blowing out the tubes on the move. Over one large rut, blow turned to suck and a capillary tube was swallowed fortunately without ill effect. On another occasion specimens were brought from Hambantota to Katunayake in a 3½ hour dash to be flown to England only to be told by the customs officer "Don't open it' just put it on the plane. I cant stand the sight of blood."

Analysis shows that the incidence of the deficiency is highest in the Anuradhapura district over the non malarious western seaboard and southern province. Study of the subpopulations shows that the migrants have the same incidence as the rest of the country whereas the purana villagers, have a very high incidence. The Ceylon Moors are the descendants of arab traders and carry the same deficient trait. They stayed with the Sinhalese in the malarious areas whereas the Tamils remained in the north only coming to the NCP later as government servants and traders. Of 160 males tested, none were deficient. These figures confirm the theory of natural selection of this enzymopathy by Malaria.

Unfortunately the security situation did not permit studies of the populations of the Malarious eastern province. The therapeutic problems that arose from the use of Primaquine, which is vital for the primary prophylaxis of the disease could

now be solved easily because it is only the purana villager, *our baiyya,* who needed to be given the reduced dosage schedule. These good people are easily identified by their courtly manners, their loud stentorian speech, special modes of dress and unusual vocabulary. They have been asked to look out for urine which turns to the colour of Coca Cola. These ancient villages are now surrounded and outnumbered by new settlers.

Their sons and daughters are being exposed to new mores of courtship and marriage so hopefully before long the trait will be diluted till it to longer is a constraint to the treatment of Malaria.

These findings were presented by us at the First International Congress of Tropical Paediatrics at Bangkok in 1988.

A vaccine if available will be a blessing for the poor farming communities of the third world who are the most affected by this disease and will benefit from the long lasting protection it offers. Currently the search is on for effective molecular or sub unit vaccines aimed at sporozoites, the asexual and the sexual stages. A new type of vaccine using viral DNA is being tried by Steven Hoffmann Director of the Malarial Programme at the Naval Medical R esearch Institute in the USA. DNA vaccines are cheaper more rapidly prepared, more stable, easier to transport and safer than traditional vaccines.

The blood smear for diagnosis may soon be supplanted by a dipstick method. Antibody tests are now available to distinguish between the two forms of Malaria.

A dangerous trend in Sri Lanka has been the rapid change in the vivax/falciparum ratio. Initially 33:1 in 1980 it is now 3:1. This is thought to be an index of the rapid transmission of the disease.

Dr Lionel Samarasinghe, formerly chief of the AMC described the Infant Parasite Rate IPR, also called The Transmission Index which is the rate found in infants as being an accurate estimation of the number of infections in an year. It was 17.5% in 1987, and 8.5% in 1989.

The initial call from the WHO for malaria ereadication has now been changed to one for Malaria Control.

The strategies include:-

Reduction of the total number of cases in the island.

Reduction in the number of cases of P Falciparum infection.

Reduction in the level of transmission of Malaria.

Elimination of fatal infections by early detection and effective therapy.

Control operations

Integrated vector control

Reduction of the parasite reservoir by vigourous treatment of infected people.

Environmental management such as the elimination of breeding places by drainage or filling.

The use of larvivorous fish like the indigenous aploceilus blockii *'nala handaya'* and the guppy. This latter are livebearers so that when the pools dry out, the fish will have to be restocked with the rains every year. The Aplocheilus has a short life span and lays drought resistant eggs which hatch with the rains.

Where this is not possible the spraying of larvicides like 'abate' should be used.

The use of an effective residual insecticide in human dwellings in spray cycles being carried out to coincide with peak transmission periods such as from November to February in the dry zone.

Constraints to the control of malaria

Parasite resistance to drugs in certain falciparum strains to Chloroquine has been noted and is treated with Quinine, Amodiaquine, and Fansidar.

There has, as yet, been no resistance to Fansidar in this country although resistance to this as well as to quinine has been reported in Northern Thailand and Cambodia. The Chinese drug extracted from 'Artemisia and available in IM IV and oral forms of the active principle Artemisinine is providing the last resort for these countries but accounts of its rapid action and low toxicity may indicate that it will be the drug of the future.

Vector resistance to Insecticides. Anopheles culicifacies is now resistant to DDT and is developing it to malathion and sumithion. Currently spraying is done with ICON and deltamethrine which are synthetic pyrethroids.

Constraints to insecticide spraying. Have reduced the spray rate from 90% in 1970 to 45% in 1989. Some spray teams have been diverted from the farmers hut to his chena to protect crops.

Devolution in 1989 the anti malaria campaign as a single independent organisation ceased to exist and the responsibility of malaria control devolved to the respective local bodies. These have their own priorities and the efficacy of control programs will vary from area to area.

The security situation has left an area of the country where all Malaria control measures are proceeding without supervision or feedback. Antimalarials and insecticides are being supplied to the 'uncleared areas' and spray teams work with the ICRC.

This nation has invested heavily in the development of new irrigation schemes. These served to reduce urban drift and increase production of rice. However these resettlement schemes brought with them an increase in vector breeding sites and large non immune populations. For a while it seemed as if these people, unused to the rigours of the disease would pack up and go back home but this tragedy was fotunately averted by the hard devoted work of the Mahaweli Authority

The second coming of Malaria was heralded by 440,644 positives in 1968 with a peak of 589,010 in 1970 followed by peaks and troughs with a mean of around 200 000 since with a slow downward trend.

The successful manufacturers of mosquito coils will testify that the mosquito is still around in large numbers. The population of Colombo is largely non-immune.

To conclude, how easily can we win against so may constraints.

We should have to keep ahead of drug resistance by finding new treatments with more research on drugs and vaccines.

We need new insecticides to keep ahead of vector resistance.

We need health education, public participation, foresight and a national plan for malaria control.

In all fields we need concerted and sustained human endeavour to overcome this scourge that could seriously affect much of humankind.

I would like to take this opportunity to thank the surgeon and the anaesthesiologists, the physician, nurses and airforce pilots who saved my life. I would like to thank my husband and my children, my very good relations and friends who stood by me in the hours of darkness that followed.

For this oration I would like to thank Dr Kusum de Abrew of the Department of Pharmacology, Dr Warusavitarana of the Antimalaria Campaign, Miss Premilla Gamage of the Institute of Policy Studies for their help, Mr Azam Latiff for the cartoons and Mr Madanayaka from the Postgraduate Institute of Archaelogy for the loan of slides and our projectionist Mr Samararatne for his patience.