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FACULTY OF MEDICAL SCIENCES

DR ASHA V. BADALOO | DR CAROLYN TAYLOR-BRYAN
DR CURTIS GREEN | PROFESSOR MARVIN REID
PROFESSOR TERRENCE FORRESTER
(and collaborators)

The Best Research Publication

ARTICLE: Dietary Cysteine is Used
More Efficiently by Children with Severe
Acute Malnutrition with Edema
Compared with those without



Cysteine is one of the amino acids present in dietary proteins and is used for the synthesis of body protein and other compounds such as glutathione (GSH) which is a major antioxidant/detoxicant in the body. Our research provides new and increasing evidence strongly supporting beneficial effects of cysteine supplementation in the treatment of edematous malnourished children.

Recent data by the World Health Organization (WHO) showed that malnutrition is associated with about one third of the 7.6 million deaths in children under 5 years each year. Childhood severe acute malnutrition (SAM) presents either as non-edematous (marasmus) or edematous (kwashiorkor, marasmic-kwashiorkor) forms. In addition to wasting, kwashiorkor and marasmic-kwashiorkor are characterized by abnormal accumulation of fluid called edema and other abnormalities carrying poor prognosis. So, whereas treatment of children with marasmus is straightforward, those with edematous SAM are difficult to treat and have higher morbidity and mortality. Furthermore, it is still not known why children develop different types of malnutrition. Hence, the focus of this work was to explore mechanisms underlying metabolic aberrations in SAM that could lead to improvement in treatment. This was done using stable isotope tracer methods to make direct measurements of rates of synthesis and catabolism of compounds in the body under different conditions.

It is well established that concentration of GSH is lower in edematous SAM compared to non-edematous SAM, and is associated with deteriorating clinical state. Previously, we have shown that this low concentration results from reduced GSH synthesis in association with low concentration of cysteine; and further demonstrated that GSH status was quickly restored with cysteine supplementation. Also, the resolution of edema was faster with cysteine supplementation. This led us to look at the overall body's demand for cysteine in SAM. The findings show that compared to non-edematous children, those with edema had slower cysteine production but higher utilization in synthetic pathways, hence better efficiency of utilization. Cysteine splanchnic utilization (gastrointestinal, liver, spleen, pancreas) was as much as 45% in both groups. Because proteins of the gut are rich in cysteine, and they turnover at extremely fast rates, cysteine deficiency may contribute significantly to intestinal atrophy and



impaired function that is more severe in children with edematous SAM. Also, they will need more cysteine to restore gut GSH, shown to be essential for intestinal protection. After splanchnic uptake, only 55% of the cysteine pool is available to meet the requirements of the other organs and tissues. This could have a negative effect on the overall synthesis of whole body GSH and proteins, especially those proteins rich in cysteine such as the skin and hair keratin; and may explain why the skin lesions of edematous SAM take such a relatively long time, 4 weeks to heal.

The body's pool of cysteine is supplied from the diet, de novo synthesis from methionine and from body protein. We have shown that slower total cysteine production in edematous SAM is because its release from protein is reduced and not because synthesis from methionine is decreased.

Potential impact on society

The results indicate that cysteine supplementation may contribute to earlier re-establishment of metabolic capacities and hence earlier resolution of symptoms in edematous SAM. The effect represents a reduction in morbidity that may extend to a reduction in mortality. This would not only confer health benefits, but the possibility of reducing hospitalization and overall treatment cost would be of important economic benefit because malnutrition is more prevalent in poor and developing countries.

Possible direct application of outcomes to industry and partnerships

The findings of this project strongly imply that the requirement for cysteine is not met by the quantity of protein provided by therapeutic diet in the acute phase of treatment. The recommended protein is restricted to meet the metabolic capacity of SAM and simply giving more protein can overwhelm the brittle metabolic state causing death. Therefore, feeds for the acute phase have to be specially prepared and this is often not convenient in non-specialized treatment centres. There is potential to partner with companies that make formulae for young children to develop a ready-to-use cysteine enriched formula for the critical period of acute treatment. This would warrant larger clinical trials. Although the prevalence of SAM in Jamaica has been significantly reduced, such clinical trials could be conducted in Haiti, a Caribbean country with high prevalence of SAM. Funding partnership with the private sector could be a start.

Dr Asha Badaloo is a Senior Lecturer in Metabolism. For over 20 years, she has been conducting nutritional metabolism research in different clinical states in children and adults.



Professor Terrence Forrester is a Physician, Professor and the Director of the Tropical Metabolism Research Unit. His outstanding research record includes the role of environmental factors and nutritional metabolism in the pathogenesis of obesity, hypertension, diabetes and childhood malnutrition.

Professor Marvin Reid is Physician, Professor of Human Metabolism & Community Health and Director, Sickle Cell Unit. His research interests are Clinical Trials of agents in Sickle Cell Disease as well as the metabolic adaptation of persons to chronic illnesses.

Dr Curtis Green is a Research Fellow. His primary areas of research include biochemistry, nutraceutical product development and nutritional metabolism.

Dr Carolyn Taylor-Bryan is a Paediatrician and Clinical Research Fellow. Her research interests include metabolism of macronutrients throughout the lifecycle.



MS GABRIELLE I. ANDRADE DR PAUL D BROWN

The Best Research Publication

ARTICLE: A Comparative Analysis of the Attachment of *Leptospira interrogans* and *L. borgpetersenii* to Mammalian Cells

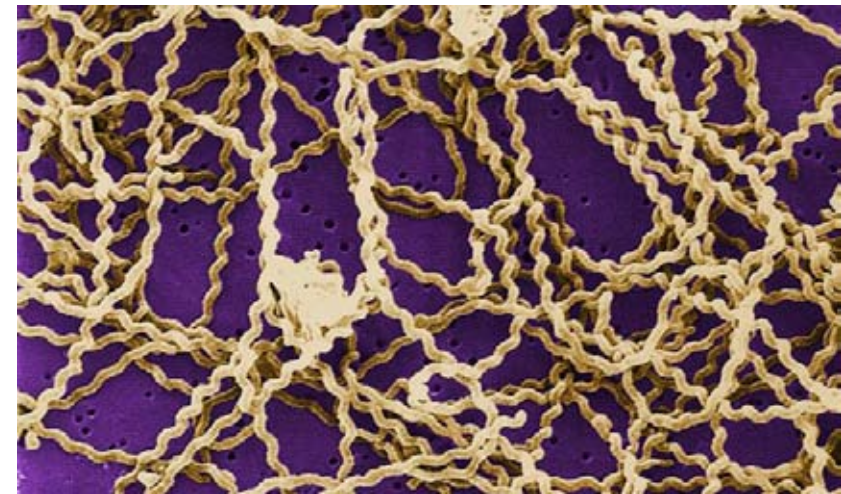


The captioned research paper evolved from the project entitled Investigation of the Basis of Attachment of *Leptospira* to Mammalian Cells, for which a grant was received from the Office of Graduate Studies and Research of the University of the West Indies, Mona Campus.

Leptospirosis is a globally re-emerging disease caused by pathogenic *Leptospira*. Since its characterization as an infectious disease in humans by Adolf Weil in 1886, annual cases of severe leptospirosis have reached 500,000, making it the world's most common zoonosis with a mortality rate of 5-20%. The disease is usually contracted through direct contact with urine, blood and organs from infected animals. Over 250 serovars that are causative agents of the disease make the development of suitable and affordable human and animal vaccines challenging for developing countries. Further, the lack of rodent pest control in slums and overpopulated urban areas, poor garbage collection, flooding, and the dependency on locally-produced agricultural products like rice and sugarcane leave third world countries at a disadvantage.

Jamaica's first reported case of leptospirosis occurred in 1953. Since then, the disease reached epidemic proportions in 1979 after heavy June floods, and a decade later serological studies showed predominant serovars to be Portlandvere, Jules, Canicola and Icterohaemorrhagiae. At the time, Jules had only been reported in Jamaica and more recent data show it has a seroprevalence of 25%, while Portlandvere has a seroprevalence of 12%. Disease incidence in Jamaica is 6 per 100,000 population, with a peak in reported cases during the second rainy season of the year, between October and December.

Clinical manifestations range from subclinical infections to full-blown Weil's disease characterized by bleeding, jaundice and kidney failure, creating a potentially fatal scenario if multiple organ failure sets in. Though recognized in Jamaica as endemic and a serious infectious disease, cases are frequently misdiagnosed and reports to the Ministry of Health are not mandatory which implies the incidence rate is grossly underreported. *Leptospira borgpetersenii* serovar Jules and *Leptospira interrogans* serovar Portlandvere are two of the bacteria that cause leptospirosis in Jamaica.



Study Rationale

The bacteria which causes leptospirosis use several known but poorly understood mechanisms to cause disease, including heat shock (or stress) proteins, lipopolysaccharides (molecules consisting of lipids and carbohydrates) and haemolysins (which cause destruction of red blood cells). *Leptospira* are not intracellular bacteria and attachment to the host tissue has been shown to be a key characteristic of the more dangerous species. In fact, because important interactions with host tissues are specific in the disease process, it is likely that there are several molecules mediating attachment of the *Leptospira* to mammalian cells. Consequently, the attachment and subsequent colonization of target organs by *Leptospira* involve a great number of interacting surface molecules on both the bacteria's surface as well as receptors on the host cell.

The Approach and Results

In this project, we assessed the attachment of the bacteria to specialized molecules known to be involved in scaffolding in tissues (such as integrins, lectins, and carbohydrates) using the human cell line HEP-2 as a model. We used a deconstruction approach for determining whether particular molecules were involved by removing them individually and checking whether that affected attachment in any way. We found that serovar Jules demonstrated better attachment to integrins tested and was not inhibited by the lectins when compared to serovar Portlandvere. Incubation with carbohydrates resulted in a decrease in attachment of the bacteria to the host cells with the exception of D-mannose in the case of serovar Jules. Both serovars generally showed a significant increase in attachment to cells after the mammalian cells were treated with enzymes.

The findings of this study suggest that some carbohydrates, including D-mannose, have an inhibitory effect on binding, which begs the question whether they could be useful in treatment of leptospiral infection in a similar way that D-mannose has been shown to be effective against urinary tract infection caused by *E. coli*. This warrants further study.

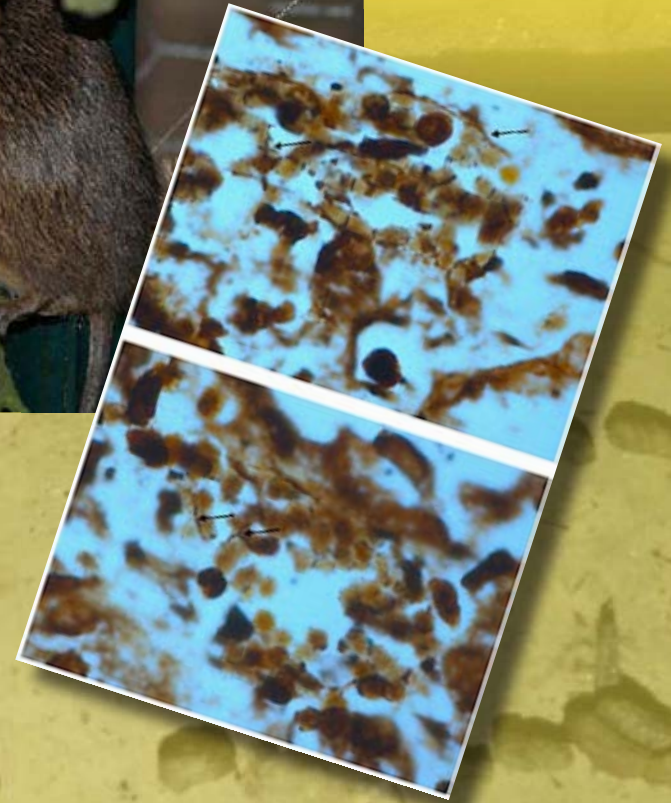
Conclusion

Taken together, these results indicate that serovar Jules tended to exhibit traits of a more dangerous strain when compared to serovar Portlandvere. When analyzed with local epidemiological data, this may explain the resurgence of serovar Jules as a leading cause of leptospirosis in Jamaica. While many will argue that clinically there is no species relatedness, epidemiologically it is critical to be able to understand trends or variations in the level of the causative agent in the environment and in clinical cases.

Ms Gabrielle Andrade is a PhD student in Molecular Biology in the Department of Basic Medical Sciences.

Dr Paul Brown is a Senior Lecturer in the Department of Basic Medical Sciences (Biochemistry Section), UWI, Mona. A Fulbrighter, he is the American Society for Microbiology Ambassador to Jamaica and is a Council Member of the International Society of Infectious Diseases.





DR LOXLEY R. CHRISTIE | DR JOHN A. HARRIOTT
DR VERNON E. DACOSTA | DR SHAUN H. WYNTER
MS DENISE M. EVERETT | MS ROCHELLE A. FOSTER

The Best Research Publication

ARTICLE: Intrauterine Insemination
in Jamaica as a Low-cost Subfertility
Treatment in Low-resource Region



Infertility affects 15% of all couples. Up to 92% of couples will conceive after a year of unprotected intercourse, the rate falling precipitously thereafter. The social burden of childlessness in resource-poor regions is clearly documented in international literature, especially on women issues. Infertile women demonstrated great risk of self-depreciation and isolation in Jamaica, were threatened with divorce in 67.7% of relationships in Pakistan and in Gambia were 3.69 fold more likely to have depression as well as being victims of abuse in up to 16.5% of relationships with husbands or in-laws. Ironically, male factors contribute to infertility as a sole cause in 28% of cases; another 28% of couples have unexplained or idiopathic infertility.

The financial burden of infertility management can also be overwhelming as no aspect of infertility investigation or treatment is currently covered by medical insurance in Jamaica. In resource-poor regions such as the Caribbean, this sentences many subfertile couples to involuntary childlessness and the associated social stigma. Provision of minimally invasive, cost effective and safe treatments is therefore a priority in these regions; Intra uterine Insemination (IUI) represents one such treatment. In vitro fertilization (IVF), an invaluable fertility technique for many couples has been available in Jamaica since 2000; however, the cost of a single IVF cycle is more than 10 times that of an intrauterine insemination (IUI) cycle.

All couples undergoing IUI cycles at the Hugh Wynter Fertility Management Unit (HWFMU), UWI, Mona from 2001 to 2005, were reviewed with intent to assess success rates and identify factors associated with successful outcomes. The couples had tried to conceive for at least one year, women had one or both fallopian tubes confirmed as being open and the men had semen analysis prior to commencing the study. Over this period, 110 couples completed a total of 161 cycles. Only patients with unexplained infertility or mild to moderate male factor infertility were chosen.

The women underwent ovarian stimulation and development of the eggs was monitored by ultrasound until they attained maturity. Semen preparation comprising a 2-step density gradient technique was conducted on specimens produced onsite. The women were inseminated with prepared sperm 36 hours



after ovulation was induced. Only pregnancies confirmed by ultrasound were considered successful.

At the HWFMU, the clinical pregnancy rate (CPR), live birth rate (LBR) and cumulative pregnancy rates were 10.1%, 8.8%, and 13.9%, respectively. These rates are consistent with CPR reports of 8.7%–18.9% from leading centres worldwide. The mean period of infertility of the patients who conceived via IUI at HWFMU (3.1 years) was mathematically significantly shorter than those who failed to conceive (5.2 years).

Women younger than 40 years of age had improved successes. Many international centres refuse to offer IUI to women over 40. In Jamaica, however, this policy has not been adopted due to the expense of IVF. At HWFMU, 23.9% of the women were over 40 years old and this negatively affected the overall success rates. Their exclusion allowed the CPR to improve to 14.9% and at the upper spectrum of results of international centres.

Males whose sperm quality improved after preparation with regards to motility and progression were found to be significantly more likely to have a successful pregnancy. Increased pregnancy rates were found among patients undergoing up to 2–3 cycles with cumulative pregnancy rates as high as 22 per cent.

The study explored the question as to whether IUI is effective in the management of subfertility or whether it serves only those who would have conceived anyway with additional time. The monthly chances of a fertile couple conceiving normally range from 15%–20%. This rate is accepted as 4%–5% among couples experiencing infertility for fewer than 3 years.

At HWFMU, the monthly fecundity rate following IUI improved to 10.1% overall and 14.9% among women younger than 40, a 2-3 fold improvement implying that IUI works. We conclude furthermore, that even if IUI serves only those who would have become pregnant anyway, it clearly results in earlier pregnancy. For couples experiencing the social burden of infertility, this may assist in saving their relationships. Failure of a series of IUI may serve to identify earlier those who may benefit from IVF.

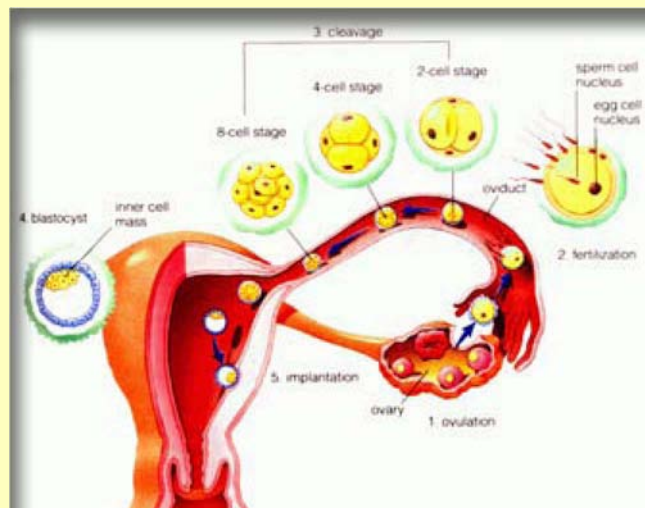
The findings of this study allow for better patient selection which will improve healthcare delivery. It allows for proper counselling of patients based on local evidence and provides clear patient selection guidelines to local doctors. It suggests IUI as an effective, safe, relatively inexpensive fertility treatment for

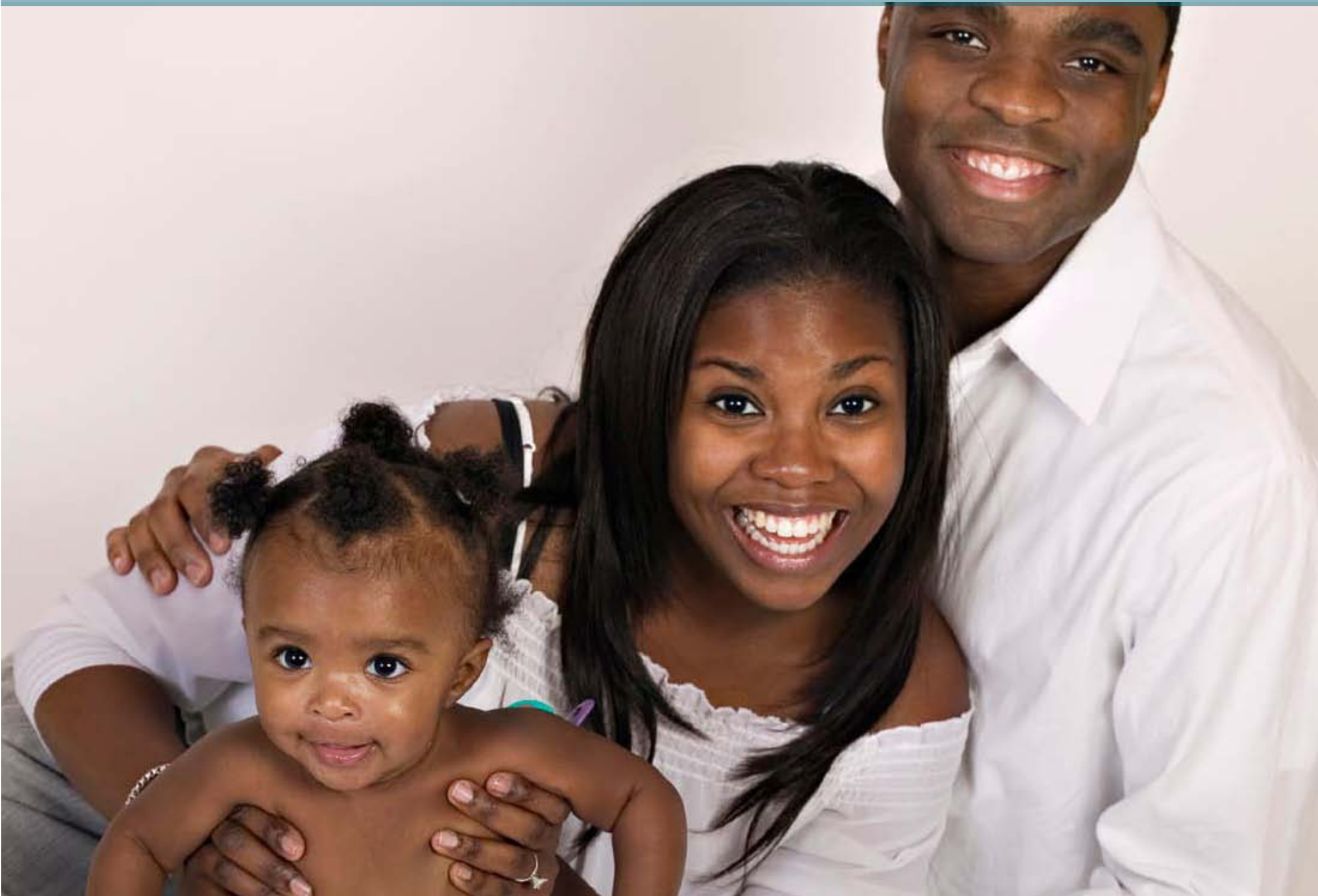
correctly chosen patients. IUI cannot replace IVF; failure of IUI acts as a guideline for selection of patients who may benefit from IVF.

This paper received an Honourable Mention in the 2011 John J. Sciarra Prize Paper Award in the category “Best Clinical Research Article from a Low/Middle-Income Country” by the International Journal of Gynaecology and Obstetrics (IJGO), the official journal of the International Federation of Gynaecology and Obstetrics. This international recognition serves to highlight the endeavors of clinicians at the University of the West Indies, limited by resources but not by intellectual and clinical capacity. This will hopefully open the prospects for further research and funding with international agencies and institutions.

Dr Loxley Christie is a consultant Obstetrician and Gynaecologist and a graduate of The UWI, Mona, who along with colleagues at the Hugh

Wynter Fertility Management Unit aims to provide excellence in fertility management through research, teaching and clinical practice.





DR MARIA D. JACKSON | DR SUSAN P. WALKER | DR CANDACE M. SIMPSON-SMITH
MRS CAROLE M. LINDSAY | MR GARRET SMITH | PROFESSOR NORMA MCFARLANE-ANDERSON
DR FRANKLYN I. BENNETT | DR KATHLEEN C.M. COARD | DR WILLIAM D. AIKEN
DR TREVOR TULLOCH | DR TOMLIN J. PAUL | DR ROBERT L. WAN

The Best Research Publication

**ARTICLE: Associations of Whole-blood Fatty Acids
and Dietary Intakes with Prostate Cancer in Jamaica**



Prostate Cancer in Jamaica

Prostate cancer is the most common cancer and the leading cause of cancer deaths in Jamaican men. Worldwide, active research efforts are taking place to identify possible causes of prostate cancer including the influence of diet and behaviour. We decided to investigate whether factors in the Jamaican diet could be associated with an increased risk of prostate cancer. However, because they rely on memory, studies of diet have been regarded to be less informative than those based on biological measurements. Measurements of certain nutrients in the blood can provide an alternative to patients' recall of dietary intake.

Does Diet Influence Prostate Cancer in Jamaica?

In this study we investigated patients' recall of their diet to determine fat intake and measured fat levels in blood as an objective measure of fat intake. We evaluated both for their association with prostate cancer.

How was this study done?

We compared 209 men, aged 40 – 80 years who were newly diagnosed with prostate cancer with 226 men of similar age who were cancer free. Both groups attended the same urology clinics. A food frequency questionnaire was used to assess dietary intake while whole-blood fatty acid composition was measured by gas chromatography.

What were the findings?

▪ Associations of whole blood fatty acids

High whole-blood monounsaturated fat (oleic acid) and moderate concentration of saturated fat (palmitic acid) were associated with reduced risk of prostate cancer whereas men with high concentrations of polyunsaturated fat (omega-3) were at increased likelihood of prostate cancer. Other fatty acids in blood were not associated with prostate cancer.

▪ Dietary intakes – nutrients

Our results showed that men who reported high intakes of monounsaturated fat (MUFA) were less likely to have prostate cancer. The principal source of MUFA was avocado. Dietary intakes of other fats did not appear to influence prostate cancer risk.



▪ **Dietary intakes - select foods and food groups**
Specific foods or food groups hypothesized to be associated with prostate cancer were examined also. Foods were grouped as unprocessed- and processed meat, seafood, fruits, dark green leafy and yellow vegetables, other vegetables (such as tomato, cabbage, string beans and cauliflower), ackee (*Blighia sapida*), avocado, beans and legumes and dairy. With the exception of intake of avocado, patients with prostate cancer reported that they consumed similar amounts of foods or food groups as did the controls. Examination of foods and food groups for their association with prostate cancer revealed that men who reported high intakes of avocado (> 60 g/day) were less likely to have the disease.

Our analysis of selected foods, food groups and nutrients hypothesized to be related to prostate cancer, found that greater intake of avocado and monounsaturated fats were associated with reduced risks of prostate cancer.

We also observed that men with a higher level of monounsaturated fat in blood were less likely to have prostate cancer. These findings are biologically plausible but need to be further studied. These findings, if confirmed, may be used to inform interventions aimed at modifying the risk factors for prostate cancer.

Acknowledgements: This work was supported by the National Health Fund, CHASE Fund and the Planning Institute of Jamaica. The authors thank the staff and participants of the study for their important contributions.

Investigators:

Dr Maria Jackson, Senior Lecturer and Principal Investigator of the Prostate Cancer Risk Evaluation (PROSCARE) study Department of Community Health and Psychiatry

Professor Susan P. Walker is the Director of the Epidemiology Research Unit, Tropical Medicine Research Institute, UWI, Mona.

Dr Candace M. Simpson-Smith, Tropical Medicine Research Institute

Mrs Carole M. Lindsay, Department of Basic Medical Sciences

Mr Garret Smith, Department of Basic Medical Sciences

Professor Norma D. McFarlane-Anderson,
Department of Basic Medical Sciences

Professor Franklyn I. Bennett, Department of Pathology

Professor Kathleen CM Coard, Department of Pathology

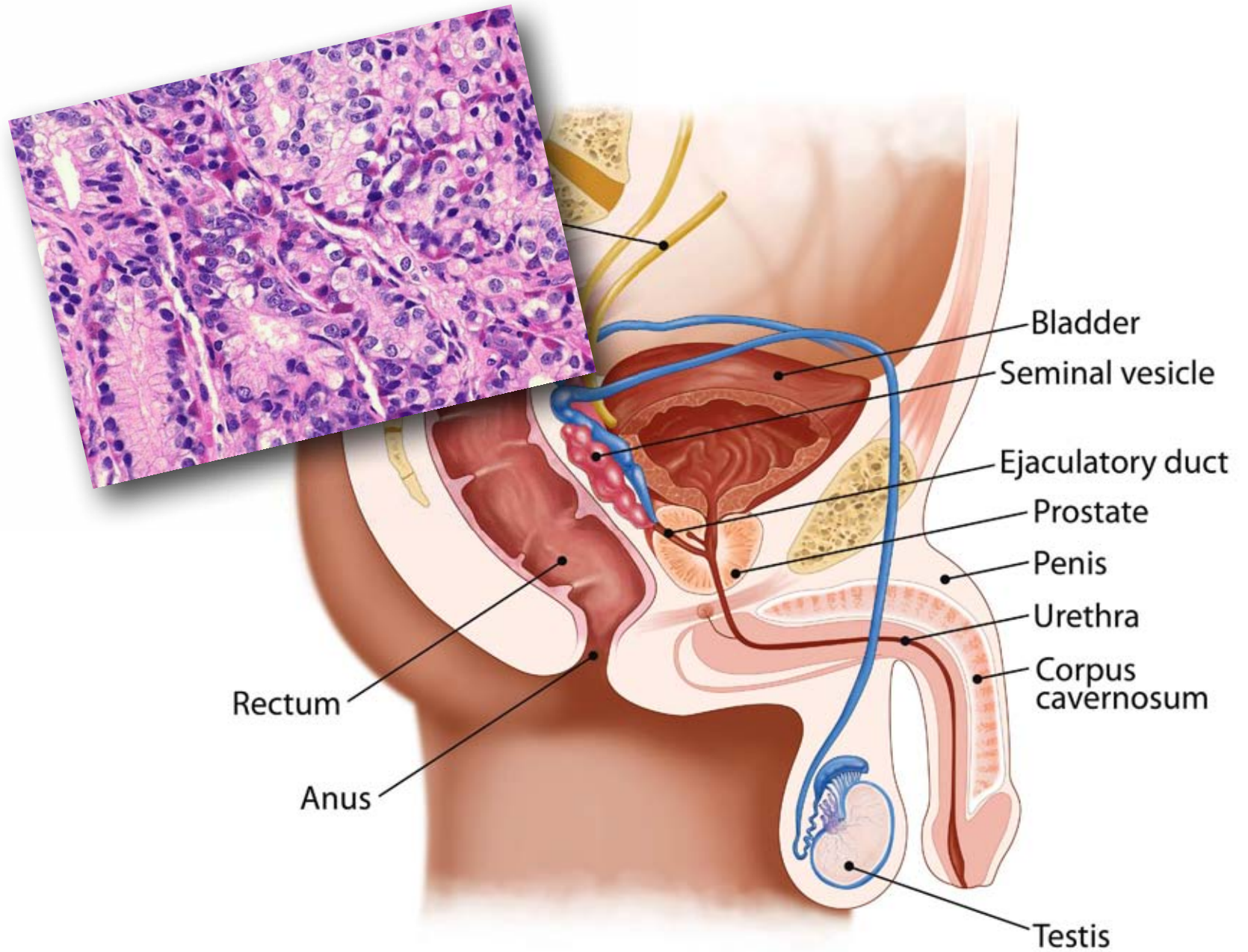
Dr Tomlin J. Paul, Department of Community Health and Psychiatry

Dr William D. Aiken, Department of Surgery, Radiology, Anaesthesia & Intensive Care.



Dr Trevor Tulloch,
Department of Surgery,
Radiology, Anaesthesia &
Intensive Care.

Dr Robert L. Wan,
Kingston, Public Hospital,
Kingston Jamaica



PROFESSOR BRENDAN BAIN | DR CAROL ANN SENAH
MS NATALIE IRVING-MATTOCKS | DR SHELLY TRIM
MRS DENISE MINOTT | DR JACQUELINE MURDOCH
MS SASHA MARTIN

**Research Project Attracting
the Most Research Funds**

**Research Project with the
Greatest Business/Economic/
Development Impact**

CHART/RCU Vice Chancellery



A Significant Landmark

April 2012 saw the achievement of a significant landmark at UWI when the CHART Regional Coordinating Unit (RCU) received a five-year grant worth US\$ 9M from the US-based Health Resources and Services Administration (HRSA) under the US President's Emergency Plan for AIDS Relief (PEPFAR). The grant, which is being called "CHART II", takes the form of a cooperative agreement with HRSA and is the first direct award from HRSA to an academic institution outside of the USA. The Unit has also received funding via regional grants to CARICOM from the Global Fund to fight AIDS, Tuberculosis and Malaria.

A Historical Note

The RCU was established in 2003 with the endorsement of CARICOM under the leadership of Professor Brendan Bain, Public Health and Infectious Disease Specialist who, at that time, was head of the Department of Community Health and Psychiatry. Since then, the Unit has grown from a staff of three to a team of 12, which now reports directly to the Vice-Chancellor. It is the central entity in the Caribbean HIV/AIDS Regional Training (CHART) Network, which has taken in-service training programmes to health care workers in more than 20 Caribbean countries, covering themes related to prevention, care and treatment of the human immunodeficiency virus (HIV) infection, other sexually transmitted infections and tuberculosis. In 2008, the CARICOM-led Pan-Caribbean Partnership against HIV and AIDS (PANCAP) named the CHART RCU as the lead agency for coordinating its capacity-building initiative in the region.

The CHART Network Partnership with I-TECH

The CHART Network began with sub-awards and technical assistance from the International Training and Education Center on HIV (I-TECH), a consortium led from the University of Washington (UW) in Seattle. I-TECH has helped with organisational development, preparation and publication of curricula and clinical guidelines, orientation of staff, and training of trainers and mentors. The receipt of the HRSA grant in April 2012 marks a transition of leadership from UW to UWI, with I-TECH expected to play a diminishing role in the partnership as the baton is passed to the RCU.



RCU and CHART Network structure and function
The RCU has served as the secretariat of a regional Executive Council and as the hub for the first CHART training centres in The Bahamas, Barbados, Haiti and Jamaica. The current team includes a training and development unit, a clinical coordinator, health information and monitoring and evaluation expertise, a human resources advisor, together with administrative and financial support staff. In 2006, a sub-regional coordinating point was established within the HIV/AIDS Project Unit of the Organisation of Eastern Caribbean States (OECS) to service that cluster of countries. The Trinidad & Tobago Health Training Centre (THTC) was launched at the St. Augustine campus of UWI in 2007 and became the newest member of the Network.

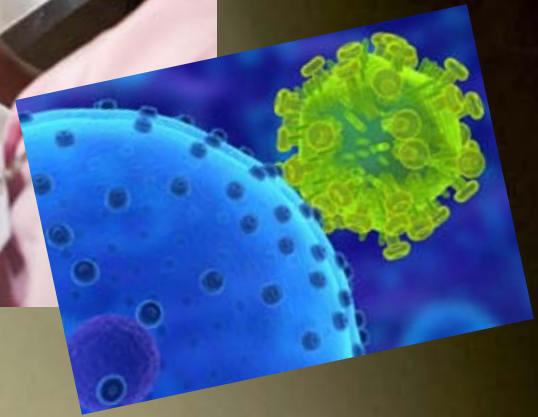
Between 2003 and March 2012, the RCU and the training centres were sub-awardees of grants received by I-TECH. The focus in the first few years (CHART I) was on training for prevention, care and treatment related to HIV, other sexually transmitted infections, tuberculosis and other complications of HIV infection. The emphasis was on increasing knowledge and skills and reinforcing professional attitudes among frontline staff who needed to respond immediately to the emergency of HIV and related conditions. In 2008, PANCAP named the CHART RCU as the lead agency for coordinating capacity building in the region.

A Wider Scope – from HIV Training to Health Systems Strengthening

Under the new CHART II programme, the scope of work will expand to include systematic health workforce development in participating countries utilizing a road map developed by PAHO and this will not be limited to HIV. The plan includes capturing the results of health sector needs assessments and providing technical assistance to participating countries and institutions as they conduct training, recruitment, appropriate placement and retention of personnel. The aim is to work with Governments, the Pan-American Health Organisation, the Caribbean Public Health Agency and other regional and international agencies to build and retain a larger human resource pool as a key component of a broader approach to the strengthening of Caribbean health systems. The results of this work will be published in the health literature.



Professor Brendan Bain has been involved in pioneering the training and practice of Clinical Infectious Diseases in the Caribbean. For the last ten years, he has led the CHART project, which is overseeing the development, monitoring and evaluation of training for health workers in more than 20 countries in the region preparing them to provide competent and empathetic care to persons infected with and affected by the human immunodeficiency virus (HIV) infection.





PROFESSOR MAUREEN SAMMS-VAUGHAN

**The Most Outstanding Researcher/
Research Activity**

ARTICLE: Autism and the Associated Risk Factors

Autism is one of the most common developmental disorders of childhood affecting one child in every 88. As this disorder is almost 5 times more common in boys, it affects one in every 54 boys and one in every 252 girls. Children with autism have delayed communication and social interaction, and unusual repetitive and stereotyped behaviours. Two-thirds of children with autism are intellectually impaired and require special education, but all children require a range of individual therapeutic services, with significant cost to parents and/or the state. The tremendous social, educational and financial impact of autism on families and public services has led to considerable research worldwide. Early research has been focussed on identifying successful interventions that improve the outcome of children living with autism.

In keeping with this, prior research at the UWI has identified delayed diagnosis when compared with children in developed countries, suggesting a role for screening and early intervention. High levels of parental stress among parents of children with autism have also been identified, with the level of stress paralleling disease severity. This suggests the need for parental support and services. Children from higher social class homes had less cognitive impairment than those from lower social class homes, suggesting the importance of stimulation in reducing disease severity.

More recent research has been focused on the identification of the cause(s) of autism, with the aim of reducing its incidence. The cause of autism is currently unknown, but 1 in 7 children have been found in international studies to have a rare genetic mutation. Environmental toxins, including heavy metals, and social environmental factors, such as advanced parental age, have also been implicated. Further, complex interactions between genes and environmental agents have also been proposed as potential causes.

Research being undertaken at the UWI to identify factors associated with a higher risk of being born with autism in Jamaica has the potential to identify causative factors, which can then inform interventions to reduce the incidence. This research in developing countries, such as Jamaica, is important in the scientific



study of causation. The identification of similar associated factors across countries with varying physical and social environments, suggests that the environment plays a limited role or that there may be unidentified environmental protective factors. Divergent associated factors across countries, however, suggest that the environment may be significant or there may be different forms of the condition.

This research project utilised the Jamaica Autism Database (JAD), established in the 1990s, for studying autism in Jamaica. The JAD includes some 600 children who have been diagnosed at public and private referral clinics at the UHWI. Some 150 children, aged 2 to 8 years from the JAD and 150 typically developing children, of similar age and gender, who had no symptoms of autism (control group), were

invited to participate in the study. Social, dietary and environmental information was obtained. Additionally, salivary and blood samples were taken for genetic and heavy metal analysis, respectively. Heavy metals, including lead, mercury, arsenic, cadmium and manganese, have been found in higher than expected levels in Jamaican soil and consequently, in foods grown in the soil.

Research Findings and Implications

Genetic and environmental analyses have been completed for approximately half of the pairs of children in the study. Jamaican children with autism had similar genetic profiles for glutathione genes and similar blood levels of mercury, lead and arsenic as typically developing children, once diet was accounted for.

The research, however, identified three times higher blood levels of lead and four to four and a half times higher blood levels of mercury and arsenic in Jamaican children, when compared with their peers in developed countries. There were also associations between blood mercury levels and dietary fish (saltwater fish, mackerel and sardines); between blood arsenic levels and dietary green leafy vegetables and non-piped water sources; and between blood lead levels and dietary shellfish and fried dumplings, as well as use of ceramic cookware and eating dirt.

Among the social environmental factors, older maternal and paternal ages, particularly over the age of 35 years, have been identified as risk factors for having a child with autism internationally. The association with parental age was confirmed in the Jamaican study. Mothers and fathers of Jamaican children with autism were approximately six years older than those of children without autism.

Public education on the increased risk of having a child with autism with advanced parental age could reduce the incidence of autism.

The research has so far identified no individual genetic or heavy metal association. Further research will investigate the gene-environment interaction and identify whether the presence of specific genes in association with heavy metal exposure increase the risk of autism. Importantly, the research has identified higher blood levels of heavy metals in Jamaican children. These heavy metals are known to be toxic to the developing brain and could impair children's learning and cognitive function. Further research to investigate any possible association between intellectual and learning disorders and blood heavy metal concentration is a priority.

The Jamaican team collaborated with researchers from the University of Texas. Some aspects of the research on autism in Jamaica were supported through grants from the NIH Fogarty International Centre and the NICHD.



Professor Maureen Samms-Vaughan is Professor of Child Health, Child Development and Behaviour, UWI; Consultant Developmental and Behavioural Paediatrician, UHWI; and Director of the Child and Family Clinic, UHWI, a referral centre for children with autism.





PROFESSOR TERRENCE FORRESTER

The Most Outstanding Researcher

**Early Life Origins of Obesity and
Associated Diseases**



The context of our research programme is, populations living in developing countries which have had intergenerational malnutrition. The focus of our research programme is, discovering mechanisms underlying the propensity of such populations to rapidly become obese and develop diabetes and other cardiovascular diseases once their economies change towards a Western model. The strategies used to discover these underlying mechanisms employ the layering of ecological contrasts of populations of African origin living in different environments, developmental biology and epigenetics.

During the past year we published some key findings related to our research goals. These findings all relate to obesity. Together, they illuminate the underlying contributions of energy expenditure through everyday physical activity, and how this important part of our ability to maintain energy balance and thus maintain our weight is altered by urbanization. In addition, we along with collaborators in five countries with African origin peoples (South Africa, Ghana, Seychelles, Jamaica and USA) laid the foundations for answering this same question in these contrasting environments where rates of weight gain vary widely. We signalled the start-up of our five-country study, comparing energy expenditure and energy intake across these populations. From these data we expect to gain an understanding of the relative contributions of energy expenditure and intake to weight gain, and importantly, the type of physical activities retained or lost that directly affect weight maintenance.

Several groups have noted that when populations that have been undernourished over many generations become more prosperous and integrated into the global capitalist economy, there is an explosion in obesity rates. We constructed a theoretical framework to explain this phenomenon and provided key evidence in support of our theory. We utilised the long history of successfully managing children with severe malnutrition at the Tropical Metabolism Research Unit to make measurements on adult survivors of malnutrition and these supported our theory that the underlying propensity to rapidly develop obesity and its associated chronic diseases, resides in fundamental changes to metabolism, physiology, and anatomy. These changes to the structure and function of the body appear to be a consequence of undernutrition in the mothers while offspring were growing in the womb, and there are early indications that severe malnutrition in early childhood exacerbates these adverse changes.

Working with collaborators in New Zealand and Singapore, we are currently engrossed in unravelling the basic mechanisms for these changes at the levels of cell biology and gene control, while looking out for opportunities to develop novel interventions based on these discoveries.

Professor Terrence Forrester is a Physician, Professor of Experimental Medicine and the Director of the Tropical Medicine Research Institute. His outstanding research record includes the role of environmental factors and nutritional metabolism in the pathogenesis of obesity, hypertension, diabetes and childhood malnutrition. He is also the convenor of Solutions for Society, a societal Think Tank established at UWI to investigate and propose tangible solutions to issues of national importance.

Research Collaborators:

Research Coordination Sandra Boyne	Nutrition Suzanne Soares-Wynter
Endocrinology Michael Boyne Debbie Thompson	Technical Bentley Chambers Diahann Knight Stacey Chin Prudence Hall
Metabolism Asha Badaloo Curtis Green Kathryn Cargill Joanne Smith	Nursing Lorraine Wilson Kenesha Pennicott-Brown Hemoy Drummond Sharon Muir Narda Steele
Clinical Carolyn Taylor-Bryan Ingrid Tennant	