

1/12 Blis in BOP schools; 2 uses, & impact on GAS!

The 20th Public Health
Summer School
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**Rheumatic fever
prevention & control:**

Update on essential issues

- **Sandra Ball** RN, BOPDHB District Nurse & Clinical Lead, ARF Eastern Bay PHA, of 4 school-based ARF prevention programmes with 3 Hauora & EBPHA.
- **Pareake O'Brien** MN, Nurse Practitioner in training, leads Kaupapa Maori Primary Health Care and Te Tohu o te Ora o Ngati Awa research partnership with EBPHA.
- **Dr John Malcolm** is a Whakatane based, BOPDHB Paediatrician

Intervention; a night time probiotic lozenge; Bacteriocin like inhibitory substances (Blis), the active ingredients in (Blis K12)

- Alpha haemolytic Strep Salivarius makes
- **2 Bacteriocin like inhibitory substances**; Salivaricin A2 and B
- Highly effective vs beta haemolytic Group A Streptococcus
- Reported by Prof J Tagg, developed with Dr J Hale and Dr P Wescombe; University Otago and Blis Technologies

- Paediatric Trials **3 months Italy** effective vs GAS
- 2013-5 Trial HRC, **12 months Porirua** Profs J Crane, M Baker
- 2015 **1 month Whakatane** schools; Ngati Awa & EBPHA

Principles behind short one month probiotic Blis K 12 course

- Italian study,
Prevented GAS 95% while taken 3/12, AND
65% in the 6 months to follow; (our emphasis)
- Discussed 2013 with Blis Otago team; **shorter time to colonize** with probiotic strains = **plausible** and BOP hope; **1/12 course may assist adherence.**

**Blis K12 probiotic lessens Kawerau
Group A Streptococcal sore throat recurrences
in school Acute Rheumatic Fever Primary
Prevention Programme 2013**

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Eastern Bay Primary Health Alliance

Nevil Pierse, University of Otago, Wellington,

John Malcolm, Whakatane, BOPDHB

The problem of multiple GAS recurrences ; Kawerau 2013, 1st GAS & recurrences

First GAS 342

Recurrent $2x=98$

Of whom $3x=48$

$4x=23$

$5x=11$

$6x=4$

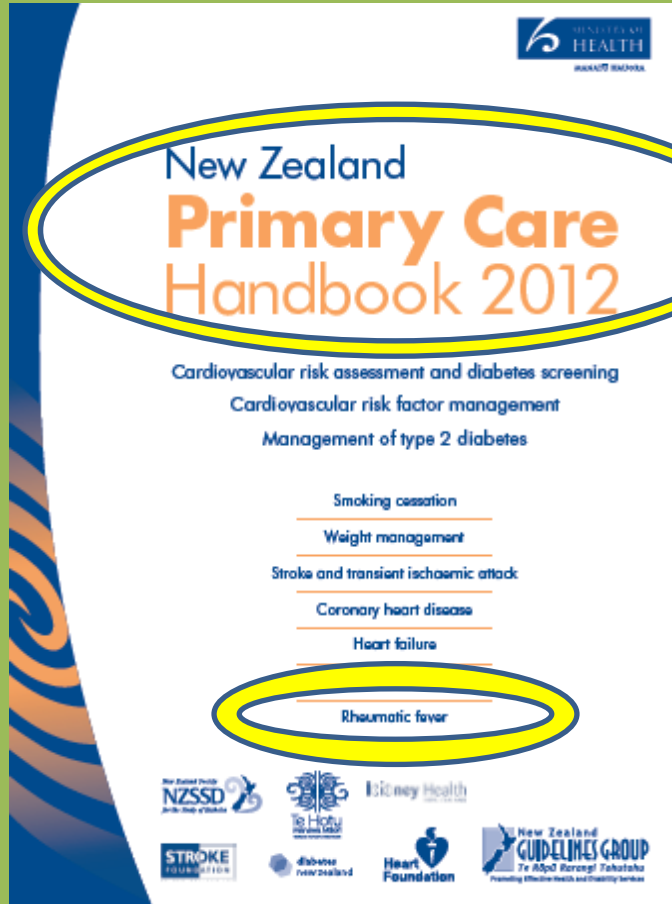
$7=1$

MOH advice Rx
Change Abiotic

BLIS 2013

BLIS 2013

Ministry of Health recurrence guide 2012 = 3 GAS sore throats in 3 months



also National Heart Foundation 2014 ; appendix 10

Antibiotic	Comment from EBOP ARF programme practice
Benzathine Penicillin	Pain /programme adherence
B or Pen VK plus Rifampicin	Specialist contact / consultation
Cephalexin	Non specialist, stewardship for staph
Augmentin	GP accessible
Amoxil 10/7 OD +Rifampicin	Specialist & stewardship of rifampicin.

Most Blis K12 was used for 3 GAS recurrences over 3-4 months

3 GAS Positive over Number of months before BLIS K12 trialed						
Number of Months	1	2	3	4	5	6
No children	0	2	7	6	1	2

BLIS K12 **course length** for 20 children

- **17** children duration **one month**
- **2** children **one month** then recurrence **then further one month**
- **1** child **one month**
then recurrence **then further two months**

Recurrent GAS Sore throat rate drops 86% after AB +1/12 BLIS K12 (Ball, BOP Clinical Research Awards 2014)

4 Months PRE BLISS Kawerau , averaged Rx GAS sore throats	3 Months PRE BLISS averaged Rx GAS Sore throats	3 Months POST BLISS averaged * Rx GAS Sore throats	4 Months POST BLISS averaged Rx GAS sore throats	6/12
3.13	2.52	0.36*	0.59	0.65
72/23	58/23	8/22	10/17 (NB 6 lost to 4/12 follow-up)	11/ 17

**(p < 0.001 @ 3/12) highly statistically significant confirmed by
Dr Nevil Piers, University of Otago, Wellington, Biostatistician**

Conclusion; BLIS K12 limits GAS sore throat recurrence for 3-5 months

- Group A Streptococcal Sore throats 86% fewer
- Blis K12 taken daily for one month, after antibiotics in Kawerau schools Rheumatic Fever Primary Prevention
- Protection significantly > antibiotics alone
- Statistical significance at 3/12, $p < 0.001$; 4/12 likely too
- **Potential Blis K12 use in recurrent GAS sore throats**
 1. **School based ARF primary prevention**
 2. **MOH Practice guideline e.g. General Practice**

ONE MONTH OF BLIS PROBIOTIC DECREASES STREP CARRIAGE & SORE THROATS IN 3 WHAKATANE SCHOOLS

Paediatric Society of NZ ASM Nov 2015

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Rheumatic Fever research intervention in 3 Whakatane schools 2015



- **History;** Previous Ngati Awa ARF promotion only contract
- **Need;** more intense ARF intervention; plan Joint venture
- **Funding;** Eastern Bay Primary Health Alliance ,Te Tohu o Te Ora o Ngati Awa EBPHA Innovation Award & BOPDHB
- **Proposal 1/Throat swab Sweep**
2/ GAS +ves, pre treat 10/7 Amoxil OD then
3/ Probiotic Blis K12 for 1 month, ALL consenting pupils

3 Whakatane Schools, high ARF risk

Mainly Maori, Education Decile 1, NZ Dep 9,10.

No ARF school sore throat swabbing programme

Te Kura o Te Paroa



James Street School



What's different in EBOP Schools; Blis trial vs sore throat swabbing

EBOP Blis Schools & AB for GAS+

- **Whole school sweep** at onset (gives prevalence)
- **Abiotic for Asymptomatic and symptomatic GAS** at start
- No weekly school sore throat swab rounds; **(6/52;3,4/12 TS)**
- **One month probiotic Blis**
- Consent 67% pupils

EBOP ARF Schools programme

- No regular whole school sweeps (*in place Auckland*)
- **Abiotic for Symptomatic GAS sore throats**; “hands up only ”
- Twice weekly sore throat swab rounds (*Auckland 3x/week*)
- No Probiotic
- Consent 97% pupils

Can 1/12 Blis lower GAS in Whakatane schools?

Method; Stepped Wedged Design; C Frampton

Power calculations N Pierce 97% consent, n 500 with 60-80% drop in GAS Carriage rate

Blis Probiotic Whakatane Schools timetable 30 July ; Plan principles; offer 3rd swab 3 months after starting to all schools and if possible to James Street and Te Oriini a 4th swab to check if the protection if strong can last 4 months.

Kura	2 ND TERM (ends 3/7/15)			3rd Term (begins 20/7 ends 25/9/15)			4 th Term	
	June	June	June & July	July & August		September	October	November
	Student & Parent Education	Consent Forms returned	1 st Swab & GAS+ Treat 10 Days	BLIS K12	2 nd Swab GAS+ Treat 10 Days	BLIS K12	3 rd Swab GAS+ Treat 10 Days	4 th Swab GAS+ Treat 10 Days
Te Kura Kaupapa Māori o Te Oriini Ki Ngati Awa	From 1/6 to 26/6	26 June	Swab Monday 29 June (x 1/7 GAS Treat)	BLIS 20/7 to 14/8	Tuesday 18 August (x 19/8 GAS Treat)	→	Tuesday 12 Oct (x 13/10 GAS Treat)	Mon, 9 Nov Then treat GAS
James Street Primary School	From 1/6 to 26/6	26 June	Swab Monday 29 June (x 1/7 GAS Treat)	BLIS 20/7 to 14/8	Tuesday 18 August (x 19/8 GAS Treat)	→	Mon 11 or 12 Oct (x 13/10 GAS Treat)	Mon 9 Nov Then Treat GAS
Te Kura o Te Paroa	From 1/6 to 26/6	26 June	Swab Tuesday 30 th June (x 1/7 GAS Treat)	→	Tuesday 11, 12 August (x 13, 14 GAS Treat)	BLIS 24/8 to 20/9	Monday 21 Sept (x 23/9 GAS Treat)	Mon 16 Nov then Treat GAS

These 3rd swab are 3/12 after Blis start

These 4th swabs are 4/12 after Blis

These 3rd swab are 3/12 after Blis start

Cornerstone of stepped wedge design is staggered start design suggested by Prof Chris Frampton Biostatistician U Otago CHCH

The swabs from James and Te Oriini AFTER BLIS need to be taken close to Paroa while still UNTREATED WITH BLIS (for the short term 1/12 Te Kura o Paroa is a control group to prove /check the point that Blis works, eg more than seasonal variation)

Findings; Blis lowers GAS prevalence 20 to 8%

- Highly significant statistics
p values & confidence intervals confirming
- Abiotics plus Blis drops GAS >> Abiotics alone
- All schools GAS prevalence was significantly less after one month Blis, and maintained three and four months later.

Significant Blis impact on GAS prevalence

“Antibiotic for GAS +ves and 1/12 Blis for all”

impact on GAS >> “Antibiotic only”

TABLE 1	Consent N	Pre Blis GAS +ves n & %	One month GAS +ves n & %	P
AB +Blis K12 Oriini + James St (OJ) Probiotic Treatment	141	27 GAS +ve of 117 swabs taken = 23.1%	11 GAS+ve of 117 swabs taken = 9.4%	<0.012
Antibiotics For GAS Paroa initial Control (PC)	162	27 GAS +ve of 112 swabs taken = 24.1%	18 GAS +ve of 112 swabs taken = 16%	=0.18

Significance		ODD s Ratio	Lower limit	Upper limit	P value
OJ after	OJ before	0.365129	0.171825	0.775902	0.01196
PC after	PC before	0.602837	0.310134	1.171793	0.182178

Lancefield Group A Streptococcus GAS declines 1,3, & 4/12 after 1/12 Blis K12

97 children at 2/3 schools swabbed at each of baseline 1, 3 and 4 months after Blis K12
The other school had 2 swabs pre Blis K12 and 1 and 3 month followup

	PRE	1/12	3/12	4/12
Number GAS Positive	GAS carriage pre Blis =22	One month post Blis =9	Three month Post Blis =5	Four month Post Blis = 5
Percentage GAS positive	22 GAS +ve of 97 swabs taken = 22 %	9 GAS +ve of 97 swabs taken = 9 %	5 GAS +ve of 97 swabs taken =5%	5 GAS +ve of 97 swabs taken = 5%
Significance P	Pre Blis compared to	<0.018	<0.001	<0.001

GAS “Sore Throats”* fewer 3/12 after Blis K12

THREE MONTH Impact GAS SORE THROATS ; prelim data 2/3 schools

Three Month results	GAS Sore throats Pre Blis K 12	GAS Sore Throats 3 month post Blis K12
2/3 school data	7 GAS +ve of 82 swabs taken = 8.5%	1 GAS +ve of 82 swabs taken = 1.2%

*** Previous results GAS prevalence symptomatic & asymptomatic
Encouraging but insufficient numbers for testing stat significance.**

Comparing outcomes in EBOP Schools; Blis trial vs sore throat swabbing

3 Whakatane schools Blis 2015

- High ARF area >> 50/100,000
- BOPDHB /MOH
NO ARF school programmes
- **1 month Blis probiotic for all**
after abiotic 10/7 for GAS +ves
- **GAS carriage 20 to 8 %**
mid year with sweep plus
antibiotic ie **AB + Blis effect**

BOP ARF Schools programme 2009-2015

- High ARF areas >> 50/100,000
- BOPDHB /MOH
ARF school programmes
- **5 year antibiotic programme**
Rx 10/7 for GAS positives
- GAS carriage 22 to 6 % 2010-14
with 2x week swabs & Kiri Ora
Rx skin sepsis 2014 (Kawerau)

Conclusions

1/ A one month course of Blis K12 probiotic achieves a useful, greater decrease in both GAS carriage (& GAS sore throats) than antibiotics alone

2/The GAS colonization decline is more rapid and greater than seasonal, summer decline in GAS.

**3/School ARF programmes*, our most effective tool, may be more effective with Blis included.
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- Whanau of the “Blis in Whakatane Schools” research team.