

A local study of radiological findings in children diagnosed with urinary tract infection

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BACKGROUND

Urinary tract infection (UTI) is a common cause of morbidity in children, requiring investigation to avoid complications. This study aims to:

describe the microorganisms grown on culture according to age at presentation

look for a relationship between abnormal US and/or MCUG results and age and clinical presentation

explore whether an abnormal MCUG was associated with abnormal US

explore whether a DMSA provides additional information to that already given by an US and/or MCUG

METHODOLOGY

All children less than 16 years of age hospitalised for upper or lower UTI, from the 1st January 2019 up till 31st December 2019 were included. Demographics, urine culture and imaging results were collected through the hospital clinical system.

RESULTS

A total of 96 children were included. *E. Coli* was the commonest causative organism across all ages. 30 children underwent both US and MCUG, whilst 14 underwent US, MCUG and DMSA. Age and clinical presentation did not highlight a statistically significant relationship with abnormal findings on US and/or MCUG. 20% of children had a normal US but an abnormal MCUG. There were no abnormal DMSA results for children with normal combination US and MCUG.

CONCLUSION

MCUG is still warranted in cases of normal baseline US, irrespective of age and gender. Given that our study was not powered enough, it was not possible to ascertain whether DMSA adds additional information in children with a normal US and MCUG. Further studies with larger cohorts are warranted with the aim of reducing DMSA referrals, radiation, and costs.

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INTRODUCTION

Urinary tract infection (UTI) is one of the commonest presentations of children to medical services and can be a significant cause of morbidity. Although most children recover fully with no further sequelae following treatment, a minority, especially those presenting with atypical or recurrent episodes, will require further investigation and follow up in order to avoid long-term complications of chronic kidney disease and hypertension.¹

Treatment with fluids and antibiotics and performing radiological studies to elucidate any underlying abnormality are mainstay in managing children presenting with a UTI. The age of presentation and type of infection, which can be classified as typical or atypical, and/or recurrent, help guide further investigation using different imaging modalities. First-line imaging investigations usually involve a renal ultrasound, a non-invasive modality that can be very useful to detect anatomical abnormalities of the renal tract such as abnormalities of kidney size and structure, evidence of obstruction or reflux (presence of hydronephrosis and/or hydroureter) and significant renal scarring. When indicated, this is then followed by more invasive imaging such as micturating cystourethrography (MCUG), which further confirms or excludes the presence of reflux, delineates the bladder outline and excludes ureteroceles or posterior urethral valves in boys; and 99mTc-labeled dimercaptosuccinic acid (DMSA) renal scintigraphy for split kidney function evaluation and detailed mapping of any renal scarring. Other radiological investigations include diethylene triamine pentaacetic acid (DTPA)/mercaptoacetyl triglycine (MAG3) renal scintigraphy, a dynamic modality that determines relative kidney function, blood flow and obstruction of the kidneys and, more recently, magnetic

resonance urography to delineate the anatomy of the renal tract. One or more of these modalities may be used depending on the issues that need to be addressed.

Although UTI is a common infection in childhood, it is estimated that only 4% of cases will have renal scarring which is visible on DMSA scans. An even smaller proportion of these cases will develop long-term complications.² Invasive radiological imaging techniques can be psychologically traumatic to both children and carers alike, with complications including exposure to radiation and introduction of infection via catheterisation in the case of MCUG. Therefore, guidelines and local protocols^{3,4} have been established to put forward recommendations for use of different modalities of imaging, with various studies examining the findings of ultrasound, MCUG and DMSA to determine the respective efficacy of each in predicting abnormalities in structure and function of the urinary tract.⁵⁻⁶

OBJECTIVES

The aims of this study are:

1. To describe the pattern of microorganisms grown on culture according to age at presentation.
2. To look at whether there is any relationship between the presence of abnormal findings on US and/or MCUG vs age and clinical presentation of UTI.
3. To explore whether an abnormal MCUG was associated with abnormalities on US, for a cohort of children who had both an US and an MCUG performed.
4. To explore whether performing a DMSA scan adds more information to that already given by an US and/or MCUG.

METHODOLOGY

Permission was obtained from the chairman of the Department of Adolescent and Child Health, the Data Protection Office and CEO office at Mater Dei Hospital.

A list of children up to 16 years of age admitted for management of UTI was obtained from departmental handover sheets, in keeping with the following inclusion criteria.

Inclusion criteria

- All children less than 16 years of age hospitalised for urinary tract infection (both upper and lower) from 1st January 2019 up till 31st December 2019.
- Only positive urine cultures obtained through clean-catch and catheter collection were considered.

Exclusion criteria

- Positive urine cultures obtained via bag collection.
- Positive urine cultures from children discharged from the Paediatric Emergency Department.

The following data was collected through the hospital electronic clinical manager system:

- Age at time of admission
- Gender
- Typical vs Atypical infection
- Culture results
- First episode of UTI vs recurrent UTI
- Result of any US – abnormal/normal
- Result of any MCUG
- Result of any DMSA

For the purpose of this study, atypical infection was defined as the presence of one of:

- Presence of an abdominal or bladder mass
- Poor urine flow
- Raised creatinine levels
- Septicaemia and serious illness
- Non-E. Coli infection on final culture
- Poor response to initial antibiotics after 48 hours

This data was collected through analysis of information documented on online investigation request forms and departmental handover sheets. Results for creatinine levels and culture results were obtained through the online hospital clinical manager system.

Recurrent infection was defined as per local protocol, that is:

- Two or more episodes of upper UTI OR
- One episode of upper UTI + one/more episodes of lower UTI OR
- Three/more episodes of lower UTI

All the above data collected was analysed using Microsoft Excel software. Chi square/Fisher test were used for interpretation of some of the results obtained.

RESULTS

Demographics

A total of 96 children were admitted during the study period. 88 (91.6%) had a UTI confirmed on urine culture analysis whilst another 8 children were treated for UTI on clinical grounds, despite this not being confirmed on culture.

Table 1 below shows the sex and age distribution of the population studied. The commonest age group requiring admission was that below 6 months of age (42.7%), with a male predominance (70.7%). On the other hand, a female predominance was observed above 6 months of age.

Table 1: Age and sex distribution of population studied

| Age group | Total (%) | No (%) of patients | |
|--------------------|-----------------|--------------------|------------------|
| | | Male | Female |
| < 6 months | 41 (42.7) | 29 (70.7) | 12 (29.3) |
| 6 months - 3 years | 40 (41.7) | 18 (45) | 22 (55) |
| 3 years + | 15 (15.6) | 4 (26.7) | 11 (73.3) |
| Total (%) | 96 (100) | 51 (53.1) | 45 (46.8) |

Culture Results in different age groups

Figure 1 below demonstrates culture results across the different age groups. E. Coli was the commonest causative organism across all age groups (61.5%). This was followed by Klebsiella in children less than 6 months of age (7.3% of infections within this age group), Enterococcus in the 6 months to 3year age group (10% of infections in this age group), and ESBL-positive E. Coli in children older than 3 years (13.3% of infections in this age group).

Correlation of Imaging Findings with Age and Presentation of UTI

A total of 96 renal ultrasounds, 31 MCUGs and 24 DMSA scans were performed. The commonest abnormality reported on US was unilateral hydronephrosis (11.5%), that on MCUG was bilateral vesicoureteral reflux (19.4%) and that on

DMSA was bilateral renal scarring with a smaller left kidney (12.5%).

Table 2 summarises the data collected for imaging results for different presentations of UTI across the different age groups. The first column shows the number of abnormal ultrasounds (irrespective of MCUG results for a particular child), whilst the second column represents the number of abnormal MCUGs (irrespective of US result for a particular child). The third column represents the total number of normal US and MCUG results for the sample population studied.

Not included in the table are 3 cases for which ultrasound was performed in view of UTI being diagnosed on clinical grounds (culture result contaminated/negative) and therefore, could not be categorised into the groups below. All ultrasounds for these latter 3 cases were normal.

Figure 1: Figure showing culture results for the different age groups. “Mixed” refers to contamination in sampling, “Negative” refers to children treated as UTI based on history and clinical symptoms despite negative culture, and “Multiple” refers to more than one organism being recorded in the laboratory culture report.

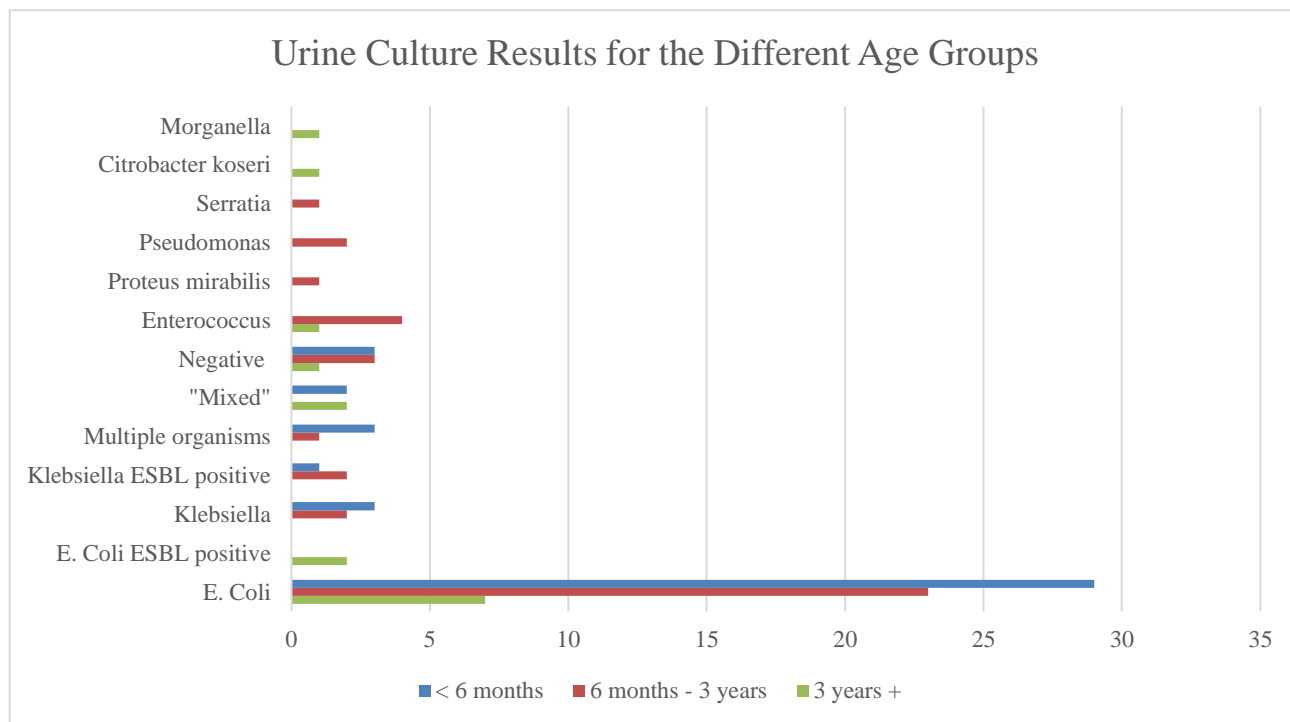


Table 2: Summary of Data Collection

| | Abnormal US Number (%) | Abnormal MCUG Number (%) | Normal US + MCUG Number (%) | Total US and MCUG performed |
|--------------------|---------------------------|--------------------------------|--------------------------------|-----------------------------------|
| Typical | | | | |
| < 6 months | 5 (10.4) | 4 (8.3) | 39 (81.2) | 48 |
| 6 months - 3 years | 6 (23) | 2 (7.7) | 18 (72) | 26 |
| 3 years + | 3 (42.9) | 0 (0) | 4 (66.7) | 7 |
| Atypical | | | | |
| < 6 months | 0 (0) | 1 (14.3) | 6 (85.7) | 7 |
| 6 months - 3 years | 0 (0) | 0 (0) | 3 (100) | 3 |
| 3 years + | 1 (33.3) | 0 (0) | 2 (66.7) | 3 |
| Recurrent | | | | |
| < 6 months | 1 (16.7) | 1 (16.7) | 4 (66.7) | 6 |
| 6 months - 3 years | 7 (35) | 4 (20) | 9 (45) | 20 |
| 3 years + | 1 (25) | 0 (0) | 3 (75) | 4 |
| Total | 24 (19.4) | 12 (9.7) | 88 (71) | 124 |

General Observations

The highest number of ultrasounds and MCUGs were performed for children presenting below 6 months of age, accounting for 49.2% of all investigations performed. 35% were performed for children between 6 months to 3 years of age and 11.3% for children aged 3 years and above.

Table 3 below allows for a more clarified description of patterns observed during analysis. Imaging studies performed in cases of typical infection yielded most abnormal results in children less than 6 months of age, very closely followed by the 6 months – 3 years age group, whilst imaging performed for recurrent infections, yielded most abnormal imaging results for children falling within the 6 months to 3 years category. Of note, for

children above 3 years of age presenting with first episode typical UTI, ultrasound revealed newly diagnosed PUJ stenosis for one child and hyperechoic bladder with debris or possibly a blood clot for another child. There were no abnormal MCUG results within this category.

Abnormal Findings on US and/or MCUG vs Age

The highest number of abnormal imaging results were reported for the 6 months to 3 years age group at 54.3%. This was followed by 34.3% for children less than 6 months of age and 11.4% for children above 3 years of age. However, further analysis of such data showed that there was no significant statistical association between the presence of abnormal imaging findings on US or MCUG and age at presentation, with a p value of 0.07 (Table 4).

Table 3: Total number of abnormal US and MCUG results (irrespective of individual results for a particular child) for different ages according to UTI presentation type. Shaded boxes indicate the highest number of abnormal results for the respective age group.

| Age | Number of abnormal US and/or MCUGs | | |
|---------------------------|------------------------------------|----------|-----------|
| | Typical | Atypical | Recurrent |
| < 6 months | 9 | 1 | 2 |
| 6 months – 3 years | 8 | 0 | 11 |
| 3 years + | 2 | 1 | 1 |
| Total No. all ages | 19 | 2 | 14 |

Table 4: Summary of the total number of abnormal and normal results (irrespective of individual results for a particular child) according to the different age groups

| Age Groups | Abnormal US/MCUG Number (%/age group) | Normal US/MCUG Number (%/age group) | Totals |
|-----------------------|---------------------------------------|-------------------------------------|------------|
| < 6 months | 12 (19.7) | 49 (89.3) | 61 |
| 6 months - 3 years | 19 (38.8) | 30 (61.2) | 49 |
| 3 years + | 4 (28.6) | 10 (71.4) | 14 |
| Total all ages | 35 (28.2) | 89 (71.8) | 124 |

Abnormal Findings on US and/or MCUG vs Presentation

Table 5 below summarises results categorised solely according to clinical presentation. Analysis of the total number of abnormal results obtained on US or MCUG (grouped together), irrespective of individual results for a particular child, showed that:

There was no statistically significant association between the presence of abnormal imaging findings in children presenting with atypical infection when compared with those presenting with typical infection ($p=0.73$).

On the other hand, a statistically significant association could be ascertained for the presence of abnormal imaging findings for children presenting with recurrent infection vs those with typical infection ($p=0.026$).

However, when both the atypical cohort and the recurrent cohort were analysed together, no statistically significant association with the presence of abnormal imaging findings ($p=0.13$) could be ascertained.

Moreover, when the number of abnormal US and the number of abnormal MCUG results was

analysed separately against UTI presentation type, there was no statistically significant correlation between the two, with a resulting p value of 0.63 for both imaging modalities.

Analysis of US vs MCUG results for children with both modalities performed

30 children had both an US and MCUG performed (1 child did not have a recent US performed despite a recent MCUG). Table 6 below summarises data for this cohort of children, comparing the results of these two modalities. Analysis shows that 20% of children (6 / 30) in this cohort had a normal US result but a significant abnormal MCUG result - 2 children had bilateral high-grade reflux, 1 had bilateral reflux with grade not reported, 2 had unilateral grade I/II reflux and 1 child had bladder wall thickening raising the suspicion of posterior urethral valves. This represents a rate of 26.67% with a lower confidence interval of 12.98 and an upper confidence interval of 46.17.

Moreover, further detailed analyses showed that there was no statistically significant relationship between findings on US and MCUG irrespective of age and gender.

Table 5: Summary of imaging results vs UTI presentation type irrespective of age

| UTI presentation | Abnormal US/MCUG | Normal US/MCUG | Totals |
|--------------------|------------------|----------------|--------|
| Typical | 20 (23.52%) | 61 (57.48%) | 81 |
| Atypical/Recurrent | 16 (37.2%) | 27 (62.8%) | 43 |
| Totals | 36 (29%) | 88 (71%) | 124 |

Table 6: Number of children categorised according to their MCUG and US result

| | US Abnormal | US Normal | Totals |
|---------------|-------------|-----------|--------|
| MCUG Abnormal | 2 | 6 | 8 |
| MCUG Normal | 7 | 15 | 22 |
| Totals | 9 | 21 | 30 |

Analysis of DMSA results for children who had DMSA performed in addition to US and/or MCUG

14 children had all three imaging investigations performed (US, MCUG and DMSA). Table 7 describes the data obtained for the cohort of children who had a DMSA performed in addition to an US and/or MCUG. Imaging results were available for a total of 22 children; 2 DMSA results were not available during time of data collection despite

being performed. 63.6% had a normal DMSA result despite an abnormal US and/or MCUG result, with a 95% CI 0.43 - 0.80. Moreover, there were no cases for which an abnormal DMSA was obtained on a background of a normal US and MCUG. Despite this, given the small cohort of children studied, this represents a rate of 75% with an upper confidence interval of 0.75, and therefore, no statements can be made as to whether a DMSA can be avoided in such cases.

Table 7: Number of children categorised according to their US/MCUG and DMSA result

| | Abnormal US or MCUG | Both US & MCUG Normal | Totals |
|---------------|---------------------|-----------------------|--------|
| DMSA Abnormal | 4 | 0 | 4 |
| DMSA Normal | 14 | 4 | 18 |
| Totals | 18 | 4 | 22 |

DISCUSSION

Radiological imaging studies have an important role in the investigation and management of children admitted with urinary tract infection. Such imaging studies in many countries generally include renal ultrasound in the first instance, followed by MCUG and DMSA when indicated. Various studies have been performed attempting to predict the yield of renal scarring and its associated morbidity using different imaging modalities, alone or in combination, for different clinical scenarios, with the aim of advocating against the use of invasive imaging techniques such as MCUG and DMSA in certain instances.^{7,8} The aim of this study was to explore whether similar proposals can be put forward for our local centre, with the aim of reducing unnecessary referrals, burden of radiation and costs.

General Demographics

A total of 96 children were included in this study, for which biochemical data, urine culture results and imaging reports were reviewed. The commonest age group requiring admission during the study was children less than 6 months of age. This was expected given that such children are more susceptible to being clinically unwell and require the administration of intravenous antibiotics and urgent imaging as per local and international guidelines. A predominance of male children was observed in this age group, similar to other studies performed in centres abroad, and this can also be explained by the higher prevalence of congenital renal tract anatomical abnormalities such as posterior urethral valves in males.⁹ Circumcision, which is known to reduce urine infections in certain cohorts, is not prevalent in our culture and only performed for specific indications, commonly for posterior urethral valves. It is also well known that there is then a marked female preponderance beyond the 6-

month age group, explained by the presence of a shorter female urethra and therefore, a higher incidence of ascending infection, as also demonstrated in this study.¹⁰

Pattern of Culture Results

E. Coli infection was the commonest causative organism across all ages, followed by *Enterococcus faecalis* and *Klebsiella pneumoniae*. This pattern in culture results is also mirrored throughout the literature in various studies performed in other centres, as highlighted by Kaufman *et al.*¹¹ Interestingly, in our study, children between 6 months to 3 years of age had most atypical infections compared to the other age groups. Given that a relationship between the presence of underlying renal tract abnormalities and atypical presentation is well-established and reported, including in studies previously performed locally, this would also explain why the number of abnormal US and MCUGs were highest within this age group accounting for 54.3% of abnormal imaging results obtained.¹²

Imaging results according to age and presentation of UTI

In this study, as also widely reported in the literature, the commonest abnormality on ultrasound was found to be unilateral hydronephrosis, that on MCUG was found to be bilateral high-grade reflux, whilst that on DMSA was found to be bilateral renal scarring with a smaller left kidney.¹³

Children between 6 months and 3 years of age were reported to have the highest number of abnormal imaging results, which could also be related to the increased prevalence of atypical and recurrent infection within this age group. This was followed by children less than 6 months of age, mainly for typical infection. Children above 3 years of age had the lowest number of abnormal imaging results, as

expected, given that the majority of UTIs within this age group are usually due to secondary factors such as constipation or potty training.¹⁴

For children above 3 years of age, ultrasound and/or MCUG (only 1 MCUG was performed within this age category for a 12 year old girl presenting with findings suggestive of acute right focal pyelonephritis on ultrasound) were performed for 86.7% of cases with 69.2% being normal. 30.8% of ultrasounds performed within this age category were abnormal, however, further in-depth analysis revealed that only one child had a newly diagnosed underlying renal tract anomaly (newly diagnosed PUJ stenosis) whilst the others were already known cases (known case of left duplex kidney with new onset mild to moderate hydronephrosis) or had an incidental acute presentation suggestive of upper UTI, requiring further imaging investigation in order to confirm this (right sided pyelonephritis).

However, despite these patterns, no statistically significant relationship could be ascertained between the presence of abnormal imaging findings on US and/or MCUG, presentation of UTI and age, and therefore, despite various guidelines highlighting consideration to age and/or presentation type to guide further investigations for most cases, vigilance is always encouraged in order to avoid missing out important underlying abnormalities that might lead to avoidable complications and increased morbidity.

Comparison of different imaging modalities used in parallel

In this study, three different imaging modalities, namely US, MCUG and DMSA were compared. When analysing abnormal imaging results for the cohort of children who had both an US and MCUG performed, 20% were found to have a significantly abnormal MCUG result (2 children had bilateral high-grade reflux, 1 had bilateral reflux with grade

not reported, 2 had unilateral grade 1/2 reflux and 1 child had bladder wall thickening raising the suspicion of posterior urethral valves, despite a normal US result. Therefore, despite various centres advocating avoiding MCUG in cases of a normal baseline US, the same cannot be said for our local centre, irrespective of age, gender and presentation of UTI.⁹

This study also aimed to explore whether performing a DMSA scan adds additional information to that already given by an US and/or MCUG. Various centres are recommending the combined use of US and MCUG to safely exclude renal scarring, with a false negative risk of 3.0%.⁹ In our study, there were no abnormal DMSA scan results for children with previously normal US and MCUG results. Moreover, 63.6% of children had a normal DMSA result despite abnormal US and/or MCUG result/s. In view of the small cohort of children studied, no statistically significant statements could be made as to whether a DMSA can be avoided in cases of combined normal US and MCUG. However, given these results, studies with larger cohorts of children are encouraged with the aim of exploring whether DMSA can be avoided in such cases locally similarly to centres abroad.

Limitations of the study

The main limitation of this study is the small number of children studied. Moreover, further studies with larger cohorts, spanning a longer time span, with more in-depth analysis of the past medical history and clinical information of the children being investigated, might highlight additional confounding factors that might be affecting the results being presented.

CONCLUSION

Invasive radiological imaging techniques such as MCUG and DMSA can be psychologically traumatic

to both children and carers alike, with complications including exposure to radiation and introduction of infection via catheterisation in the case of MCUG. The results of this study suggest that in our local centre, MCUG is still warranted in cases of normal baseline US, irrespective of age, gender and presentation of UTI. Moreover, in view of the small cohort of children studied, it was not possible to ascertain whether performing a DMSA can be avoided in cases of normal baseline US and MCUG. However, given that in our study, all children with normal US and MCUGs had normal DMSA scans and 63.6% of children had normal DMSA scans despite abnormal US and/or MCUG, further studies with larger cohorts of children are warranted with the aim of reducing referrals for DMSA, unnecessary radiation burden and costs.

SUMMARY

What is known about the subject

1. Urinary tract infection is a common cause of morbidity in children.
2. Investigation of UTI in children often involves imaging including ultrasound, MCUG and DMSA scans.

3. Various guidelines have been put forward to guide imaging investigations in children depending on age and clinical presentation of UTI.
4. Various centres advocate avoiding MCUG in case of normal baseline US and avoiding DMSA in cases of normal combination US and MCUG results.

New findings

1. E. Coli infection was the commonest in our studied cohort, similar to studies performed abroad.
2. In our local centre, MCUG is still warranted despite normal baseline US irrespective of age, gender and type of presentation.
3. Further local studies with larger cohorts are warranted in order to ascertain whether a DMSA can be avoided for children with normal combination US and MCUG.

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